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PATHOLOGIC CHANGES IN DISEASES OF JOINTS*

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THE pathologic changes in diseases of the joint, so far as they are related to roentgenology, are most important. It is doubtful whether all interpretations of roentgenograms are based on actual pathologic studies. What I shall present here is essentially a summary of work already presented,[1] and a review of 120 pathologic specimens of resected joints studied at The Mayo Clinic during the last three years.[4,5] In both of these investigations the specimens and the roentgenograms were studied together. In the later study, because all of the material was composed of resected knee joints, it was possible to make fairly accurate comparisons between the roentgenograms and the specimens.

In a consideration of the pathologic changes in diseases of joints there are perhaps three phases which should be covered: gross pathologic changes, microscopic pathologic changes, and changes of unknown origin. Among the latter the change which seems to me the most important is in the calcium content of bone or in atrophy of bone. Although much has been learned regarding this condition in the last few years, it may still be said there is much to learn. When the many problems concerning the physiologic chemistry of tissues of joints and bones have been solved, then this problem will be solved.

In no other diseases are descriptions of the pathologic changes in the joints so accurate as in tuberculosis of the joints. König[8] gave us our present-day conception, and although he, as well as many other observers, dwelt more than modern writers on the differentiation of the gross pathologic stages such as hydrops, fungous and purulent lesions, yet his descriptions of the gross as well as microscopic changes hold good today. Much futile argument has passed regarding the situation of the primary lesion, whether in bone or synovia. It should be recognized that, except in an occasional case, at the time the diagnosis is made the disease is actually found in the cancellous bone adjacent to a joint and also in the synovial membrane of the joint. The only practical application of the discovery of purely synovial tuberculosis would be in the ability to cure the local disease by synovectomy, a procedure which will rarely be successful in tuberculosis. The second fact of importance in tuberculosis is that at the time diagnosis should be made the roentgenogram rarely shows sufficient changes to lead to a diagnosis. By exclusion the roentgenogram may be of aid in these early stages, but it is then rarely possible to detect positive changes. The same may be said of diseases of most joints. However, this does not belittle the importance of the

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roentgenogram. In most instances the disease has advanced to the point where definite roentgenologic diagnosis can be made at the time the patient presents himself to the physician.

In tuberculosis the lesion is primarily destructive. Although there is marked proliferation of tubercles throughout the synovial membrane and often extensive proliferation of tubercles in the cancellous bone, this proliferation leads also to destruction of cartilage and bone. The most common picture of a tuberculous joint is that of excessive synovial pannus or tuberculous proliferation involving, as a rule, the entire synovial membrane and covering a large portion of the surfaces within the joint, which are not subjected to pressure. The bone is more or less extensively affected with tuberculous tissue invading the spaces within the trabeculae, breaking down trabeculae here and there, and in some areas coalescing to form bony cavities which may or may not be caseous and ultimately break down and suppurate.

The cartilage, although often partly preserved over a long period, is slowly destroyed. Its destruction comes about mainly in two ways: from the pannus which overgrows its surface, sending granulation tissue into its depth at intervals along the surface, and from subchrondral granulation tissue which undermines the cartilage, sending buds of tissue into the cartilage at various points. These two processes, progressing simultaneously, ultimately choke out the cartilage. Caseation of tubercles is seen in many cases. The exact cause of caseation is not clearly understood. It was formerly thought to be due to lack of circulation or ischemic necrosis. Krause, however, decided that caseation is not an ischemic process but rather "an end result of the inflammation with which the allergic reaction is initiated." The significance of this allergic reaction is emphasized by Krause, who demonstrated its development in the experimental animal and its significance clinically. That there is some definite sensitization of cells is undoubtedly true. The formation of the tubercle is in itself a manifestation of the sensitivity of the cell.

PROLIFERATIVE ARTHRITIS

It seems heretical to speak of tuberculosis and proliferative arthritis in the same breath; nevertheless it is my purpose to draw a parallel picture between these two conditions based solely on the pathologic changes. Clinically the picture of the two conditions is perhaps rarely confused, but I wish to emphasize the similarity in many respects which may be found on studying the pathologic changes and the roentgenograms, when but one joint is pictured (Fig. 1). The similarity rests on the following changes:

1. The changes in the synovial membrane in proliferative arthritis are characterized by focal collections of small round cells and reticular cells, often simulating tubercle but not containing the epithelioid cells which are characteristic of the tubercle. These focal collections of cells must represent some specific cell sensitization or change similar to that seen in tuberculosis, and which in its broadest sense must represent some allergic state.

2. The cartilage in proliferative arthritis may not only be covered by a pannus but may be the seat of definite subchondral infiltration by granulation tissue somewhat similar to that seen in tuberculosis.

3. Marginal erosion of bone may take place such as is often seen in tuberculosis (Fig. 1).

4. Atrophy of bone usually occurs and the bone is often the site of small focal collections of cells similar to those seen in the synovial membrane.

DEGENERATIVE AND TRAUMATIC ARTHRITIS

These two processes are identical in their early stages. The earliest pathologic change noted is degeneration of the matrix of the cartilage with increase in the definition of the fibrils leading later to actual fibrillation. With this goes a change in the car-

tilage cells, which become irregular in size and arrangement. Increased calcification in the deeper layers of the matrix is common. The secondary changes in bone are more or less dependent on the extent of this degenerative change; if it is recent, there is little change in the underlying bone, but if it is advanced, marked thickening of the underlying trabeculae or subchondral plate occurs, this process being extended to frank eburnation if the cartilage is completely destroyed. In both types the synovial membrane shows simply fibrosis, with more or less thickening of the walls of the vessel.

Such conception has been elaborated by Lang in a recent article. He stated that the only satisfactory explanation for arthritis deformans is found in the functional theory of Pommer. "This theory presupposes that the joint cartilage through its elasticity protects the subchondral bone and its marrow from the irregular localized effects of impacts, jarrings and pressures arising from normal function. Following damage to the joint cartilage, with subsequent loss of its elasticity, the mechanical effects of normal joint function become more or less localized and are transmitted unmodified to the joint structure resulting in a reactive vascularization and ossification of the cartilage." Lang further pointed out the relationship to strain, and stated: "Arthritis deformans is already initiated in the early years of life and therefore, the disease has to be considered as a consequence of trauma carried over from childhood and adolescence."

a *b*

Fig. 1. *a*. Tuberculosis of knee of three years' duration. Marginal erosion, and thickening and atrophy of soft parts may be noted; *b*, proliferative arthritis, picture similar. In both of these cases the diagnosis has been established by microscopic examination and the cases have been observed for a long time after operation.

a *b*

Fig. 2. *a*. Knee joint the site of osteochondritis dissecans in the external condyle. Very little change can be seen; *b*, roentgenogram with the knee flexed. Extensive injury to the joint surface of the external condyle of the femur is shown.

The variations in this process can be seen in the clinical extremes. Any joint which has been the site of trauma, either acute and severe or mildly chronic will show these changes. They are most marked in advanced cases of morbus coxae senilis and comprise late changes in hips, the seat of Legg-Perthes' disease in early life, or those in advanced cases of slipped epiphysis. Any joint which has been the site of a fracture may manifest a similar change and many purely traumatic lesions of joints fall into this category.

PYOGENIC JOINTS

The pyogenic infections of joints include a group of cases which may vary remarkably in appearance at the time the patients consult the clinician, surgeon, or roentgenologist. This variability depends on the

virulence of the infection and on the duration of the symptoms. There is, however, probably more uniformity of pathologic change in this type of infection than in any other. Phemister[11,12] has shown the means by which digestion of the articular cartilage takes place in pyogenic infections. He pointed out that it is partly due to proteolytic ferments derived chiefly from the leucocytes, partly due to absorptive action of granulation tissue and partly to erosion of the opposing articular surfaces. Thus the change in the cartilage in these cases is of prime importance in understanding the pathologic changes. In the more active types of infection the cartilage softens early and in microscopic sections invasion of this softened cartilage by polymorphonuclear cells may be seen. At the same time the synovial membrane becomes thickened with edema of the subsynovial layers, the vessels become engorged and thickening of the membrane varies according to the duration of the infection. On the surface of the synovial membrane may be seen fibrinous exudate often containing many of the blood elements but particularly polymorphonuclear cells. In the deeper layers are various stages of organization with vascularization. The bone in the earliest stages of a purely suppurative joint, is not involved, but as the deeper layers of the cartilage become involved, infection shows itself in the bone or it may spread directly to the bone from the reflexion of the synovial membrane at the circulus articuli vasculosus. The marrow spaces of the bone become packed with polymorphonuclear leucocytes and bacteria. Death of the bone may ensue unless the infection subsides. This may be only partial or, as is often the case if patients are young and particularly if the hip joint is involved, an entire epiphysis may become a sequestrum due to such an infection.

The most serious pathologic change which may be interpreted in the roentgenogram is swelling of the synovial pouch. The second serious change is narrowing of the joint space. This change must always be observed carefully because of the distortion due to position, amount of flexion deformity and so forth. If roentgenograms of opposite joints are taken in exactly the same position or if stereoroentgenograms are employed, definite narrowing may be observed and used as a diagnostic point. In the more advanced cases of this type of disease, such a change is invariably seen. Because of the fairly rapid and extensive destruction of cartilage this type of disease most often leads to ankylosis of joints, which is in contradistinction to tuberculosis, with which ankylosis rarely ensues. It should be pointed out that a tuberculous joint in which there is secondary pyogenic invasion, may thus become ankylosed. Furthermore, when a tuberculous joint becomes so infected the characteristic picture of tuberculosis is often completely destroyed. Remnants of tuberculosis may be found here and there, but one may often search extensively for tuberculous changes and not find them, yet tuberculosis is present.

Besides the usual types of infecting organism such as *Staphylococcus aureus*, *Staphylococcus albus* and the streptococcus, there are many other less common invaders. Among these should be mentioned the pneumococcus, and influenza bacillus. Gonococcal infection of joints, so far as the pathologic changes are concerned, are practically the same. Here again there may be rapid destruction of cartilage leading in many cases to ankylosis, although if the infection is arrested early, so that cartilage is not destroyed, ankylosis does not take place.

LOOSE BODIES IN JOINTS

The formation of loose bodies or joint mice may be due to one of three conditions: osteochondritis dissecans, synovial osteochondromatosis and traumatic internal derangement either with or without arthritic changes. In the latter group belong those cases of arthritis in which loose bodies become separated and cause symptoms. In this case the arthritic changes may be said

to be primary and they are usually degenerative. In the other types of loose body formation there is always present some arthritic change, the result of injury to the articular surface produced by the loose body. Such arthritic changes are always traumatic and follow the line of development of that type of arthritis. In cases in which the loose bodies have existed for a long time the secondary changes may become extensive so that they obscure the original lesion.

Osteochondritis dissecans is a name given by König[7] to a condition found usually in adolescence and young adult life, and is characterized by the apparent spontaneous separation of a piece or pieces of bone and its covering cartilage from the joint surface. The separated fragment varies in size and there may be more than one fragment consisting of a piece of cancellous bone covered with its articular cartilage. The bony surface is covered with a layer of fibrous tissue, often fibrocartilaginous. The lining of the cavity is usually smoothly covered with a layer of fibrous tissue. These so-called loose bodies may not be loose but may be retained in situ by the cartilage, or this may be only partially intact, acting as a hinge which allows the loose piece of bone and cartilage to move in and out of its bed.

Although the typical case presents a picture somewhat as described, there are many variations. In some instances the separated portion may be composed entirely of cartilage. There are instances in which separation of the cartilage from a large portion of joint surface may take place without other etiologic factors. The loose bodies may appear in the external condyle (Fig. 2) or in the hip, elbow, ankle, or shoulder; I have seen one case in which there appeared to be such a formation in the head of a metatarsal bone.

There are many hypotheses with regard to the origin of loose bodies. Wolbach and Allison in post-mortem study of a case of osteochondritis dissecans found cystic degeneration of the cancellous bone underlying the area of loose body, so that the articular surface had caved in over this cavity. The cavity was not depicted in the roentgenograms, which lends strength to the hypothesis that it may exist in other cases even though the roentgenograms fail to show such cystic change. There are also cases in which this condition is superimposed on an old epiphyseal lesion, such as Legg-Perthes' disease. It usually occurs among young subjects, and always in epiphyseal bone.

Synovial osteochondromatosis is an entirely different condition, so far as etiology is concerned. In this condition multiple loose bodies are produced. In the early stage they may be cartilage, but in later stages they are of bone as well as of cartilage in many instances and many of them are pedunculated. Their origin is accurately described by Jones. The consensus of opinion seems to be that it is a benign tumor or a degenerative process involving the synovial membrane only.

Loose bodies, due to traumatic internal derangement either with or without arthritic changes, are not so spectacular from the standpoint of etiology. These are more commonly seen in cases of degenerative arthritis in which with or without trauma a fragment of bone or a bony spur may become detached and lie within the joint. Thus the etiology in these cases is arthritis and trauma. The number of such loose bodies may vary, although they are never so numerous as those seen in synovial osteochondromatosis.

ATROPHY FROM DISUSE

This condition should be considered a definite syndrome, although it is not always recognized by clinicians. It usually occurs following trauma of more or less severity, when overtreatment and overfixation have resulted in a painful joint whose only abnormality may be atrophy of the muscles and of the bones, as demonstrated in the roentgenogram. Occasionally the lining of the joint may be thickened or there may even be effusion into the joint, al-

though this is usually seen only after overuse. The pathologic changes of this condition, as would be expected, are chiefly atrophy of all the tissues. The bone is definitely atrophied with thinning and diminution in the number of the trabeculae. The cartilage, too, is definitely thinned, with fewer cartilage cells in its deeper layers. Evidence of pannus having formed may sometimes be seen, but there is little active proliferation.

CALCIFICATION OF SEMILUNAR CARTILAGES

This condition is somewhat rare and may be seen usually coincidental to some other condition for which roentgenograms have been made. It is doubtful whether calcification will in itself cause symptoms. The cause, so far as I am aware, is entirely unknown.

TUMORS OF SYNOVIAL MEMBRANE

Synovial osteochondromatosis might be included in this group, but it has already been described in a consideration of loose bodies. Besides this condition xanthoma is probably the most common tumor of synovial membranes. It has been described under various names, xanthoma being the one most commonly used in this country. Joints may be secondarily involved from tumors of bone. There are several cases of tumor of the capsule of the joint reported by Enderlen. It is difficult to determine in these cases whether the tumor originated from the ligamentous tissues making up the capsule or from the synovial membrane, but it would appear that at least some of these tumors were fibrosarcomas originating in the ligamentous capsule. Other tumors of the synovial membrane which have been reported are foreign body giant cells, angiomas, and fibromas. In this connection cysts of the semilunar cartilage may be mentioned. These are not strictly tumors although certain observers contend their etiology to be congenital cell rests in the cartilage. Others believe them to be of traumatic origin. They are more commonly seen in the external semilunar cartilages. Roentgen diagnosis is usually not possible unless the cyst is of considerable size.

Tumors of the synovial membrane have been considered by Faulkner and by Talbot, both of whom have given excellent bibliographies. Faulkner was able to find 29 cases in which 25 tumors were in the knee joint. Ten of these tumors were xanthomas. In 3 cases metastasis and death occurred; and in 4, subsequent amputation was necessary. In none of these articles is there a consistent roentgenographic picture of the condition.

The tumors arising from the joints or their adjacent structures, as observed at The Mayo Clinic in the last ten years, have been reviewed. In 12 cases the tumors apparently arose from the synovial membrane or its subsynovial layer. These cases were diagnosed as follows: benign xanthic tumors with giant cells, 6 cases; giant cell tumor, 1 case; hemangioma, 1 case; hemangioendothelioma, 1 case (patient dead); endotheliosarcoma, 2 cases (1 patient dead), and myelosarcoma, 1 case (patient dead).

In none of these cases was a positive diagnosis made by the roentgenogram. Usually the shadow in the roentgenogram was of soft parts. In 3 cases some secondary erosion of bone had taken place.

ARTHROPATHY

Neurotrophic arthropathy is a lesion of joints not often described. I have observed the pathologic change in 2 such cases. The gross pathologic picture is that of extensively injured articular cartilage. Many loose fragments of bone and cartilage are found in the joint. The synovial membrane is thickened, but without any characteristic changes except fibrosis. The microscopic appearance of the articular surface shows marked distortion of the cartilage where it remains, increased calcification of the deeper layers of the cartilage, and the subchondral plate with thickening of the trabeculae. The pathologic physiology of this condition is, I believe, not understood.

SUMMARY

A pathologic picture of the more common types of lesions affecting the joints is presented. These lesions vary greatly not only from other types of lesions of the joints, but often, so far as the roentgenogram is considered, the same lesion taken in different stages will appear almost entirely different. It is pointed out that the ideal time to make a diagnosis of disease of the joints is before lesions can be detected roentgenologically. This, however, is not often possible, and many patients present themselves for an opinion only after the disease is well advanced and after definite changes can be demonstrated roentgenologically.*

* For discussion see page 795.

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CORRELATION OF PATHOLOGICAL AND ROENTGENOLOGICAL FINDINGS IN THE DIAGNOSIS OF TUBERCULOUS ARTHRITIS*

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A KNOWLEDGE of the pathology of tuberculous arthritis in its various stages is essential for detailed interpretation of the changes shown in roentgenograms of such joints. Both the pathological and the roentgenological pictures in adults differ somewhat from those seen in children because of the difference in structure at the two ages. There may also be differences according to the joint involved depending on the amount of contact of opposing articular surfaces and the amount of weight bearing. One of us (D.B.P.[1]) has previously reported on changes as seen in adults.

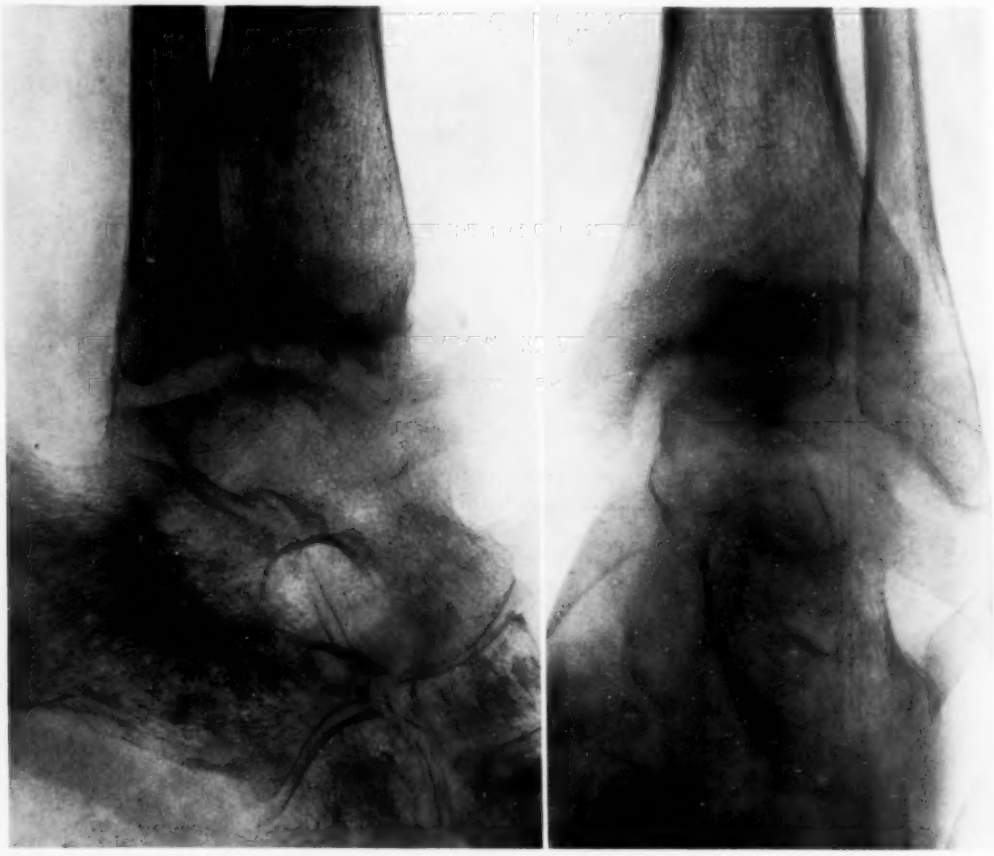

FIG. 1. Case 1. Shows regional atrophy and loss of shadow of bony articular cortex in ankle joint with preservation of cartilage space of joint. The uninvolved joints show preservation of shadow of both articular cortex and of cartilage space. Shadow of periosteal new bone on surface of tibia.

Tuberculous arthritis may be primary either in the synovia or in the bone. At the time of the roentgenological, or particularly the pathological, examination it is usually

* From the Department of Surgery of the University of Chicago. Read at the Thirty-third Annual Meeting, American Roentgen Ray Society, Detroit, Mich., Sept. 27–30, 1932.

difficult to determine where the primary focus was located. A small primary focus in the bone may extend to the joint and set up tuberculous arthritis without being detectable in roentgenograms of the joint. Changes in the ends of the bones secondary to the tuberculous arthritis may be so extensive that it is impossible to distinguish them from primary osseous lesions, even on pathological examination of the resected joint. More extensive and detailed pathological and roentgenological studies of tuberculous joints than any heretofore published will be necessary before the exact percentages of primary osseous and primary synovial forms are known. Koenig's[2] extensive statistics showed the primary lesion somewhat more frequently in the synovia than in the bone, but they are unreliable in that they were not aided by roentgen studies.

TUBERCULOUS ARTHRITIS IN ADULTS

Primary synovial tuberculosis soon spreads from the point of onset diffusely over the lining membrane producing tuberculous granulation tissue. This tissue then attempts to grow over the free surfaces of articular cartilage and absorb it. Contact of the opposing articular surfaces and motion in the joint tend to prevent the overgrowth. If the tuberculous process is relatively mild the granulation tissue remains alive and continues to overgrow and destroy articular cartilage over long periods of time. If the process is severe there may be early necrosis of the granulation tissue before it has overgrown and produced extensive surface destruction of the articular cartilage.[3] As the tuberculous arthritis becomes more advanced subchondral granulations develop in the entire extent of the articular cartilages, gradually absorbing bony articular cortex and loosening articular cartilage which is also thinned by absorption from beneath. Microscopically the subchondral granulations consist largely of fibroblasts, round cells, and macrophages, and are nearly always free from tubercles. The presence of this nonspecific, subchondral granulation tissue is probably best explained on the assumption that the articular cartilage is killed partly by interference with its nutrition from the synovial fluid and partly by the action of tubercle toxins, after which it forms largely as a foreign body reaction to sequester and absorb the necrotic cartilage. In joints such as the hip and ankle in which the opposing articular cartilages fit accurately and are extensively in contact, the articular cartilage is most extensively destroyed by subchondral granulations, there being relatively little marginal overgrowth and erosion of the free surfaces by the time that the cartilage is completely detached.

The roentgen findings in such tuberculous joints at this stage are fairly typical and usually consist in three changes: (1) there is regional atrophy of disuse; (2) there is reduction or loss of density of the shadow of articular cortex due to bone absorption by the subchondral granulations, and (3) there is preservation of the cartilage space of the joint. The loosened articular cartilages may persist for many weeks or months. This is because of the absence of proteolytic ferments[4] in the tuberculous exudates to digest them and because of the slow rate of attack and absorption of cartilage by the subchondral granulations after it has been detached. The following is an illustrative case:

Case 1. J.K., male, aged nineteen, complained of pain, swelling and impaired function of the left ankle for eight months with a sinus anteriorly for two months. A roentgenogram of the ankle (Fig. 1) shows regional atrophy, almost complete loss of the shadow of bony articular cortex of the ankle joint and presence of cartilage space. A shadow from slight periosteal new bone formation on the lower end of tibia is present. The uninvolved subastragalar and mid-tarsal joints show presence of cartilage space of joint and also shadow of bony articular cortex.

Diagnosis: Tuberculosis of ankle.

Operation: Through a Kocher lateral incision the ankle joint was exposed. Tuberculous synovitis was present and granulations had slightly overgrown and eroded the margins of

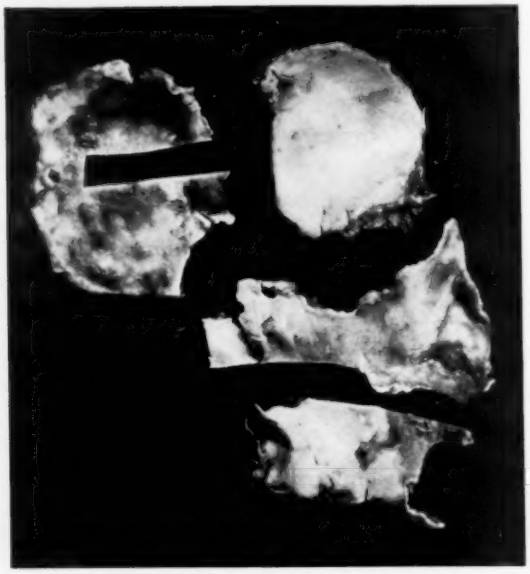

FIG. 2. Case 1. Shows articular cartilages which were found almost completely undermined and detached from bone.

the articular cartilage especially on the anterior portion of the astragalus. The cartilages were partly detached, the remaining bony attachments being easily separated. Joint fusion with tibial grafts was done. Figure 2 shows a photograph of the resected cartilages.

Microscopic examination showed the free surface of the astragalar cartilage overgrown at its periphery anteriorly by granulations in which could be found many tubercles and giant cells. The cartilage was extensively detached from the subchondral bone by granulation tissue containing many round cells, but no tubercles or giant cells. Buds of this granulation tissue had invaded the deeper portions of the cartilage in many places.

The patient also complained of slight occasional pains in the right shoulder for one month. A roentgenogram revealed an essentially normal shoulder joint. One year later the patient returned with a successfully fused ankle but with a stiff and painful shoulder which had been acutely painful only for a period of two weeks. A roentgenogram (Fig. 3) revealed regional atrophy, loss of the shadow of bony articular cortex with slight subluxation and slight narrowing of cartilage space. An area of reduced density was present in the region of the greater tubercle. A faint shadow of periosteal new bone is seen on the mesial side of the neck of the humerus.

FIG. 3. Case 1. Shows regional atrophy, loss of shadow of bony articular cortex on head and glenoid, narrowing of cartilage space, slight subluxation in joint, diminished density of shadow of greater tubercle and slight shadow of periosteal new bone on mesial side of neck of humerus.

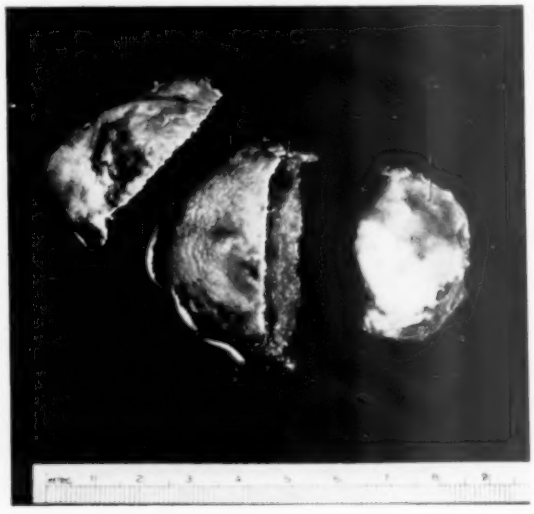

FIG. 4. Case 1. Photograph of detached articular cartilage of glenoid (*a*) and of humerus (*b*) restored on portion of resected head (*c*).

Operation: Resection of shoulder and bridging of joint with two full thickness tibial bone grafts. Extensive tuberculous synovitis was found with much caseation. The articular cartilages were completely detached and markedly thinned but still in situ. The cartilages were removed and the major portion of the head of the humerus was chiselled away. A large tuberculous cavity in the greater tubercle was curetted. Figure 4 is a photograph of the detached glenoid cartilage (*a*) and a cross section of the capital cartilage (*b*) reapplied to the excised portion of the head of the humerus (*c*). The bony surface denuded of cartilage showed a thin surface layer of granulation tissue. Figure 5 is a microscopic section of this reconstructed excised portion of the head showing loosened and thinned necrotic cartilage (*a*), subchondral granulation (*b*) and markedly atrophic bone (*c*). One year later the shoulder was solidly fused.

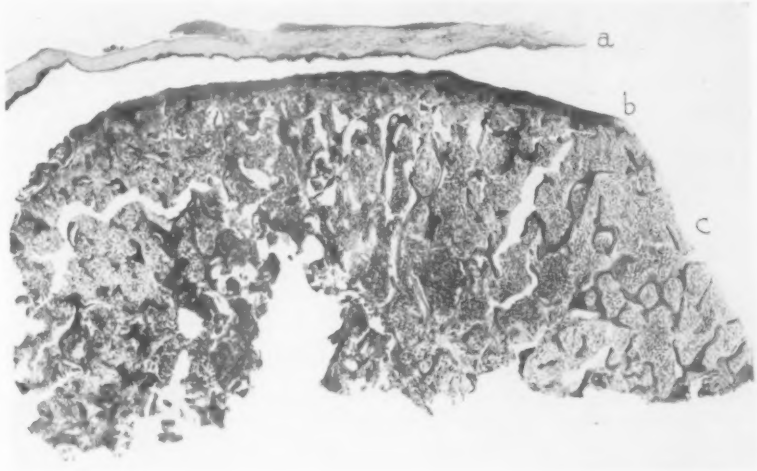

Fig. 5. Case 1. Microscopic section of head of humerus showing detached necrotic cartilage (*a*), subchondral granulations (*b*) and atrophic bone (*c*).

With time the articular cartilages are gradually thinned, softened and finally destroyed. This stage may be recognized in roentgenograms by narrowing or even complete disappearance of the cartilage space of the joint, as exemplified by the following case:

Case II. M.C., male, aged thirty-six, had symptoms and signs compatible with tuberculosis of the hip for eighteen months, when a roentgenogram (Fig. 6) was taken. It shows marked regional atrophy and disappearance of the shadow of bony articular cortex on both acetabulum and femoral head. There is marked narrowing of the cartilage space and irregular reduction in density in the greater tuberosity adjacent to the neck.

Operation: Resection of hip and bridging of the joint with bone grafts. At operation a cold abscess and extensive caseous tuberculous synovitis were found. Articular cartilages were extensively destroyed and the remaining portions were completely detached and markedly thinned, which greatly reduced the thickness of cartilage space.

With still further advance of the tuberculous process the bones may be invaded and absorbed, and grooves and pits may be created along their articular surfaces. There may be marginal grooving of the sides of the end of the bone adjacent to the periphery of the articular cartilage. These changes are readily made out in the roentgenograms from the presence of grooves and irregular areas of reduced density. There is usually absence of sclerosis in the ends of the bones at this stage but sometimes there is periosteal proliferation on the surfaces of the epiphyses and even extending distally onto the ends of the shafts as shown in Figure 1.

In the knee joint where the flat surface

of the tibia articulates with the curved femoral condyles there are extensive surfaces of both free and contacted articular cartilage in the joint. Tuberculous granulations gradually overgrow the free cartilage surfaces and erode the cartilage from without inward. If the tuberculous granulations do not caseate and the disease is relatively mild the surface granulations may completely destroy the articular cartilage and erode the underlying bone in the noncontacted regions, while the articular cartilage and cortex are still preserved in the contacted regions. This may give rise to a characteristic roentgen appearance of preservation of the shadow of bony articular

FIG. 6. Case II. Tuberculosis of left hip with regional atrophy and loss of shadow of bony articular cortex and of cartilage space of joint.

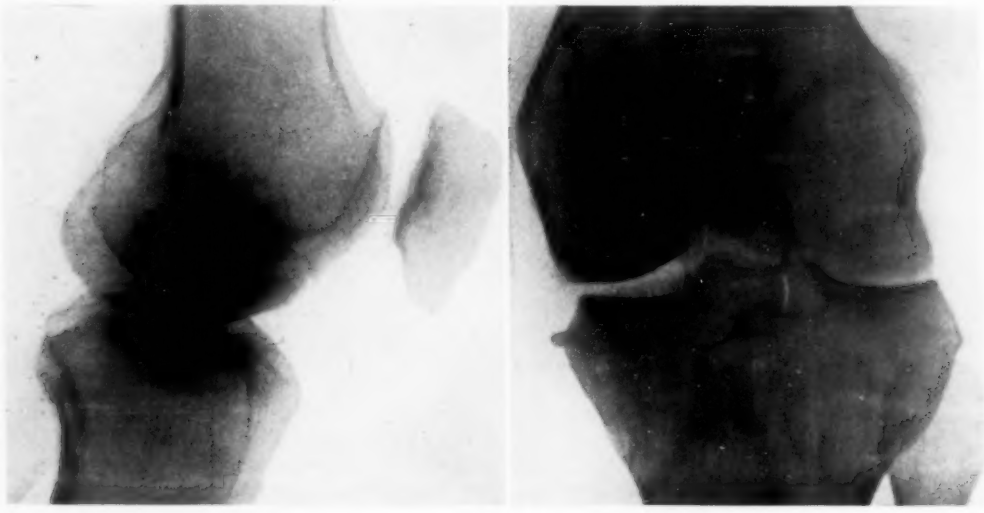

FIG. 7. Case III. Mild tuberculosis of ten years' duration. Lateral view shows loss of shadow of bony articular cortex in free regions between patella and tibia and on backs of condyles. Preservation of cartilage space in contacted regions. Anteroposterior view shows marginal destruction on tibia with spur at base of groove, cartilage space of joint preserved mesially and narrowed laterally.

cortex and of cartilage space of the joint in the contacted regions with partial or complete loss of shadow of bony articular cortex and even pitting or grooving in the non-contacted region. This is illustrated by the following case:

Case III. L.D., female, aged twenty-six, had pain and limited motion in the left knee for ten years. For one year prior to operation there had been more severe pain and swelling which at times prevented weight bearing. There had been no sinus and motion was limited to 40°. The roentgenogram (Fig. 7) shows in the lateral view loss of the shadow of bony articular cortex of femoral condyles in the unopposed regions between patella and tibia and on the posterior surface of the condyles. The cartilage space between the condyles and patella is preserved. In the anteroposterior view marginal destruction on the tibia with spur formation at the base of the groove is seen. The shadow of bony articular cortex and cartilage space are preserved in the contacted areas of the medial tibial tuberosity and medial femoral condyle. On the lateral femoral condyle the shadow of bony articular cortex is less well defined and cartilage space between lateral condyle and lateral tuberosity is thinned.

Operation: Resection of knee for fusion of joint. A photograph of the specimen is shown in Figure 8. Extensive tuberculous synovitis was present. Surface granulations had destroyed and replaced the articular cartilage and bony articular cortex over the unopposed areas. In the opposed and contacted regions of the joint articular cartilage looked softened and unhealthy but was remarkably well preserved considering the duration of the disease. On the lateral side of the joint some thinning of articular cartilage had taken place through absorption by subchondral granulations.

Massive invasion of the bone at the points of greatest contact and pressure is not infrequently seen in weight-bearing joints, especially the knee, occasionally the hip, and results in large areas of necrosis. This usually takes place before the bony articular cortex in the region has been extensively absorbed or the articular cartilage extensively loosened. The tuberculous tissue of the necrotic area usually becomes caseous and a zone of absorbing granulation tissue develops about its periphery which leads very slowly to sequestration. What happens on one side of the joint usually happens on the other, since the mechanical influences are the same, so that kissing sequestra or bilateral areas of necrosis are the usual result. They are often

Fig. 8. Case III. Photograph of specimen from resection of knee shown in Figure 7. Cartilage still present but damaged in contacted regions and destroyed and replaced in non-contacted regions by tuberculous granulations.

roughly cone shaped with their bases bordering on the articular surfaces and have usually been confused with primary lesions of the bone. The bone in these necrotic areas is usually atrophic but the atrophy is less marked than in the surrounding living bone in which it has progressed since the time that the tuberculous invasion and necrosis took place. In some instances articular cortex is preserved, while in others it is partly or completely absorbed. The roentgenologic evidence of massive invasion and necrosis of bone in the more traumatized weight-bearing portion of the joint usually consists of four changes. (1) The bone of the necrotic areas casts a denser shadow than that of the surrounding living bone because of atrophy of the living bone subsequent to the occurrence of the necrosis. (2) A line of demarcation either partial or complete is to be seen after the necrosis has existed for some time. (3) The shadow of articular cortex, of either normal or reduced density, is preserved over the necrotic areas and lost in the rest of the joint. (4) Opposed areas of necrosis are often present in the bone ends, which is evidence of their secondary nature. The following case is illustrative of these changes:

CASE IV. E.K., female, aged twenty-six, had had symptoms and findings compatible with tuberculosis of the knee for four years. No sinus. Roentgenograms (Fig. 9) reveal in the lateral view marked destruction of bone on the articular surface of the femur in the non-contacted regions between patella and the weight-bearing portion and on the backs of the condyles. But the articular surfaces of the condyles and tuberosities and patella are fairly well preserved in the regions of contact. A dense area is seen in the external condyle of the femur bordering on articular surface and a larger cone-shaped one is present in the tuberosity of the tibia opposite it. An incomplete line of demarcation is seen about the dense area in the

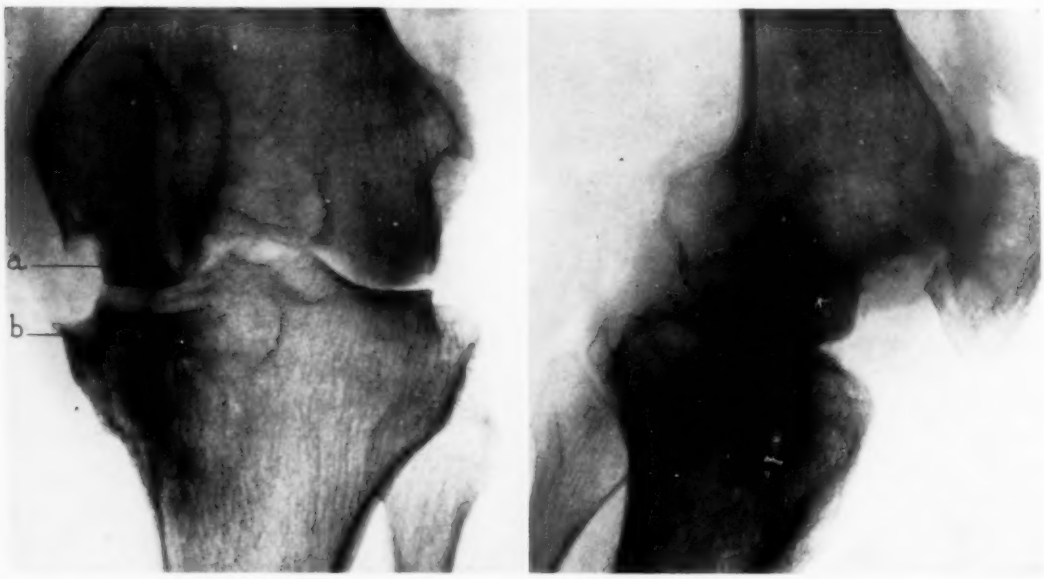

FIG. 9. Case IV. Lateral view shows extensive bone destruction in unopposed regions of condyles between patella and tibia and on posterior surfaces of condyles. Opposed areas are preserved. Sequestrum in tibia distinct, that in femur vague. Anteroposterior view shows marginal destruction, spur formation, and shadow of periosteal new bone on medial tuberosity. Opposing dense shadows (*a*) and (*b*) of bone are seen in medial condyle and tuberosity over which shadows of bony articular cortex are present and almost normal cartilage space preserved. Sequestration lines incomplete. On lateral tuberosity the shadow of bony articular cortex is present but on the lateral femoral condyle it is indistinct. Cartilage space laterally is diminished.

tibia. In the anteroposterior view these dense areas are seen more distinctly. The shadow of articular cortex is preserved on each and an incomplete line of demarcation is seen about the area in the condyle of the femur. There is grooving about the margins of articular cartilage on both sides of the tibia and on the mesial side of the femur. Mesially there is spur formation back of the grooves on both femur and tibia. There is a dense shadow of new bone formation on the mesial side of the epiphysis of the tibia. The shadow of articular bony cortex on the lateral condyle is considerably less than normal; that of the lateral tuberosity only slightly so. Cartilage space of the joint is slightly narrowed laterally, but of normal width mesially where shadow of articular cortex of the tuberosity is slightly displaced downward (on the sequestrum). Knee resection was performed. Figure 10 shows the specimens. There was extensive tuberculous synovitis with much caseation. The free articular surfaces on the femur between the points of contact with the patella and tibia and on the backs of the condyles had been overgrown by granulations which had destroyed cartilage and underlying bone and which in much of their extent had undergone caseation and liquefaction. The surfaces at the points of contact were preserved but the articular cartilage covering them was softened, thinned, and gray in color. Granulations had overgrown and partly eroded the sides of the articular cartilage of the patella, leaving only the central half of its surface free. The semilunar cartilages were extensively broken down and granulation tissue covered the margins of the articular surfaces of the tibia. The line of resection in the tibia passed through a large, white, cone-shaped necrotic and sequestrated area in the external tuberosity and that in the femur passed through the apex of a smaller and shorter one in the external condyle (Fig. 11). A roentgenogram of the resected ends (Fig. 12) shows the trabeculated bone in the sequestra to cast a slightly heavier shadow than that of the living portions. Microscopic examination of soft tissues showed the usual picture of tuberculosis.

It is generally held that marginal lipping or osteophyte formation does not occur in tuberculous arthritis. It should be remembered, however, that occasionally there is subperiosteal proliferation with lipping at the edge of the groove formed about the surface of the ends of the bones which simulates the osteophytes formed from proliferating fibrocartilage in arthritis deformans. They can be distinguished from the latter by the fact that they are situated a short distance back of instead of at the margins of the articular cartilage. Figure 7 illustrates the marginal lipping of tuberculous arthritis.

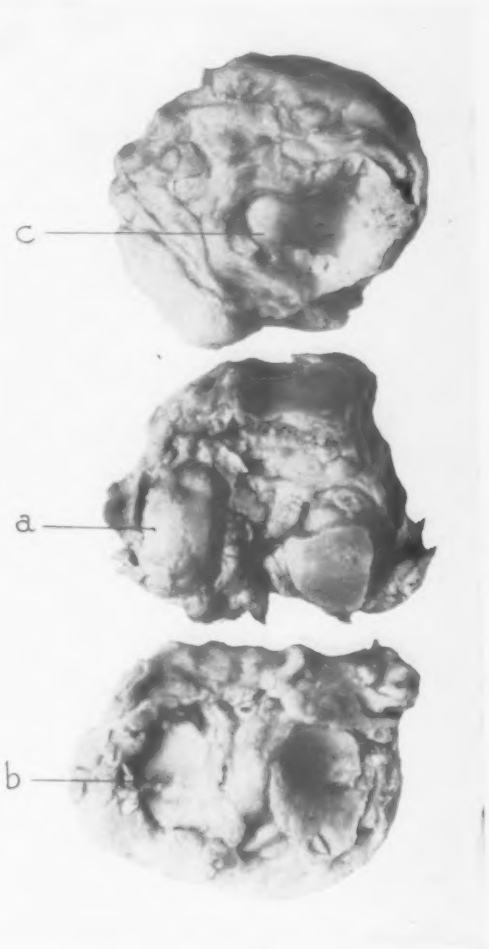

Fig. 10. Case IV. Photograph of resected knee showing replacement of articular cartilage and superficial bone by tuberculous granulations in the unopposed regions. Articular cartilage is present but badly damanged over the opposed regions. Base of sequestrum (*a*) in mesial condyle and of sequestrum (*b*) in mesial tuberosity covered by articular cartilage and distinguishable with difficulty. Patella (*c*) shows marginal encroachment of granulations on cartilage.

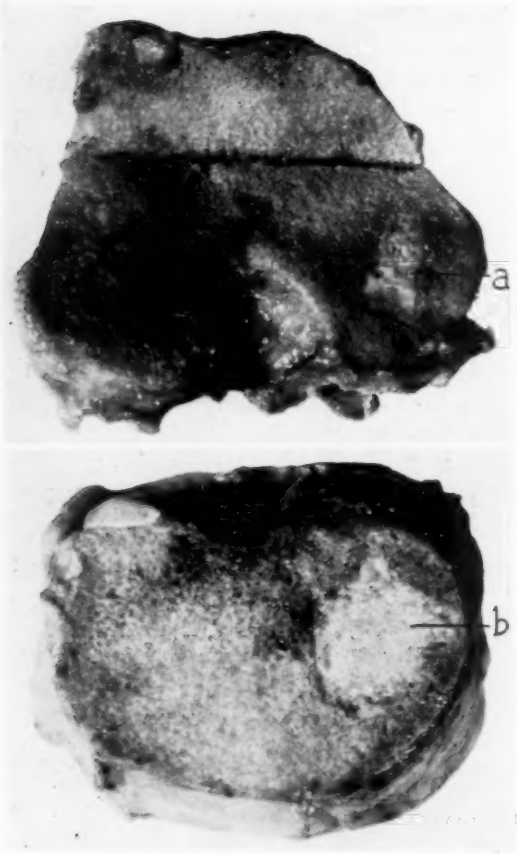

FIG. 11. Case IV. Photograph of cut surfaces of femoral condyles and tibial tuberosities shown in Figure 10. The sequestrum in medial condyle (*a*) and that in medial tuberosity (*b*) are seen.

Bony ankylosis almost never occurs when secondary sequestra are present and the tuberculous process usually remains active unless such joints are resected. Fibrous ankylosis sometimes occurs after complete destruction of articular cartilage and cortex with more or less erosion of the underlying cancellous bone. The tuberculous process may be quiescent but is rarely healed and recurrences are likely to occur. Sclerosis of bone ends and occasionally bony ankylosis will take place under favorable circumstances. The development of secondary pyogenic infection entering through tuberculous sinuses may hasten the loss of articular cartilage, especially in the weight-bearing regions, and occasionally may stimulate new bone formation. It may also aggravate the tuberculous process.

PRIMARY OSSEOUS TUBERCULOSIS

In adults, when the disease is primary in the bone, the focus is usually located in the epiphysis bordering on the joint. The infection soon extends into the joint producing changes that are identical with those of primary synovial tuberculosis. The primary osseous lesion may be very small and the area may break down with the formation of a cavity filled with tuberculous granulation tissue or necrotic débris. In that event it is easily overlooked both in the roentgenological and in the pathological examination. It may be difficult to dis-

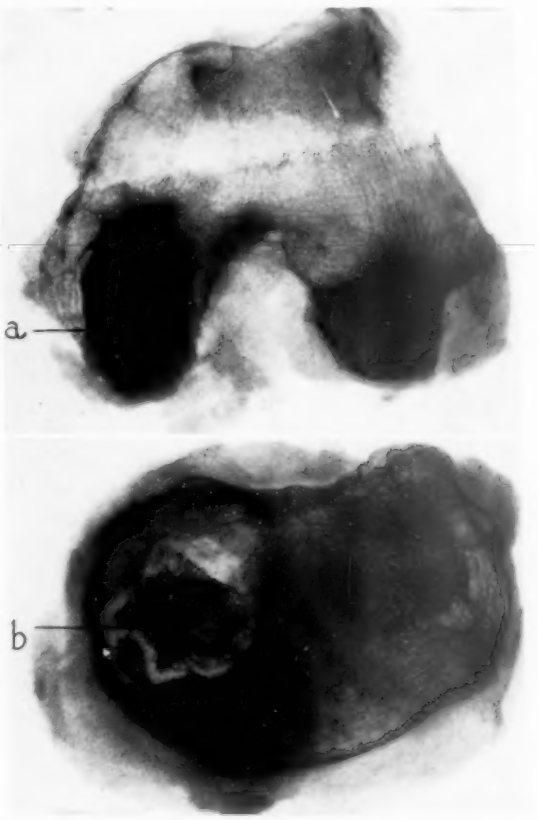

FIG. 12. Case IV. Roentgenogram of specimens showing opposing sequestra in medial condyle (*a*) and tuberosity (*b*). Density and size of trabeculae greater in sequestra than in surrounding atrophic bone. Clear zone about sequestrum represents granulation tissue separation.

tinguish between it and the secondary tuberculous lesions in the bone.

When the area is larger it may undergo caseation and sequestration. In that event the dead bone usually persists and the surrounding living bone becomes less dense, due to atrophy of disuse. Until atrophy and sequestration have set in it is usually impossible to recognize such necrotic areas in roentgenograms. Occasionally if the necrotic area borders on the periphery the overlying periosteum will form a layer of new bone. These conditions are illustrated by the following case:

Case v. V.F., female, aged twenty-one, had had symptoms of tuberculosis of the spine for one and a half years with positive roentgen findings. For two months there had been some pain and limitation of motion of the left knee and on examination slight swelling and tenderness were present. A roentgenogram (Fig. 13) showed normal findings aside from a thin layer of bony density over the mesial side of the epiphysis of the tibia. No change was made out in the underlying bone. Spinal fusion was performed and three weeks later the knee was explored. Tuberculous synovitis was found but there was as yet only beginning overgrowth of pannus on the free surfaces of articular cartilage. The synovia was excised and the ends of the tibia and femur resected. The saw cut crossed a caseous oval focus in the mesial tuberosity of the tibia, 2×1 cm., extending to the articular cartilage and to the periosteal surface of the bone. The focus had here perforated into the joint. Figure 14 shows the focus in two planes and Figure 15 the microscopic section cut coronally. The trabeculae in the necrotic portion are preserved and of about the same density as those in the living portion and the line of sequestration is only partly established. This explains why the focus in the bone was not demonstrable in the roentgenograms. There was a thin layer of periosteal new bone not shown in this microscopic section which passed through the point of perforation into the joint.

Fig. 13. Case v. Shadow of cortical new bone at (*a*), otherwise normal roentgen findings.

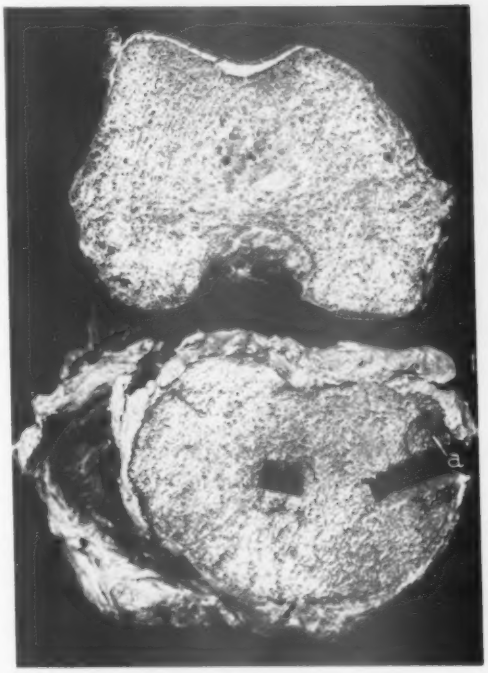

Fig. 14. Case v. Photograph of cut surfaces of resected femoral condyles and tibial tuberosities. A primary bone lesion partially sequestrated (*a*) is present in the medial tuberosity.

Primary sequestra may be differentiated from secondary sequestra by the fact that they are unilateral whereas secondary sequestra are usually bilateral, and also by their density which may be greater than that of secondary sequestra, the bone of which had atrophied before being invaded

and killed. In fact, as reported by Phemister, in some cases of secondary sequestra the density is no greater than that of the surrounding living bone because extreme atrophy has preceded the secondary invasion and sequestration. The shadow of articular cortex on the primary sequestrum is well preserved and may be denser than that of the secondary sequestrum. A primary sequestrum is likely to be more nearly cone shaped than the secondary sequestra. The cone-shaped nature of the primary sequestrum led Koenig[2] to the belief that it was the result of tuberculous infarction. However, pathological examination has not substantiated the view that primary osseous foci are always the result of infarction.

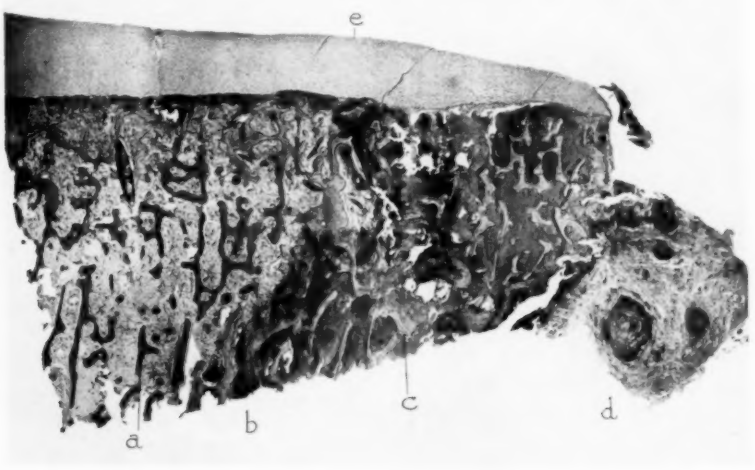

FIG. 15. Case v. Microscopic section through focus in tuberosity: (*a*) living bone; (*b*) fibrous tissue forming line of sequestration; (*c*) necrotic bone; (*d*) joint granulations; (*e*) articular cartilage.

TUBERCULOUS ARTHRITIS IN CHILDREN

In children there is some variation in the changes from those seen in adults. In late childhood and adolescence the picture gradually approaches the adult form. The disease is perhaps primary in the synovia in a higher percentage of cases than in adults. When the primary focus can be identified as osseous it is more frequently situated in the metaphysis than in the epiphysis. These statements are truer for younger children than for older ones.

A primary osseous focus is especially apt to be seen in the hip joint where it is most frequently situated in the juxta-epiphyseal portion of the neck in the distribution of the infero-mesial neck artery. The following case illustrates such a lesion:

CASE VI. B.C., male, aged eleven, had slight pain in the right hip and knee for five months. On examination motion of the hip was restricted to about half that in the normal joint. The roentgenogram (Fig. 16) shows regional bone atrophy of the right hip, an irregular area of rarefaction in the metaphyseal region within which smaller shadows of density greater than that of surrounding bone appear, and slight marginal destruction of the capital epiphysis. Cartilage space is undiminished.

Operation: Curetting of metaphyseal lesion and fusion of hip with tibial bone grafts. Microscopic sections of the synovia showed a tuberculous synovitis. On the superior surface of the femoral neck, openings in the cortex led to the cavity within the bone. This was curetted out, the material removed consisting of tuberculous granulation tissue in which many small sequestra were found. At the extreme margin of the femoral head the articular cartilage was found to be slightly undermined by granulations, but otherwise it appeared normal.

A primary osseous focus in the knee is rarely to be made out, but even there it is perhaps more frequent in the metaphysis of the femur or tibia than in the epiphysis.

The layer of articular cartilage is proportionately thicker in children than in adults and the younger the child the greater the proportion, because of the relative smallness of the center of ossification in the epiphysis. Erosion of the cartilage from granulations overgrowing its free surfaces

Case vii. P.T., a female, aged nine, had slight pain and swelling of the left ankle region for four years. For three months prior to entry there had been more acute symptoms which prevented weight bearing, but no sinus had developed. The roentgenogram (Fig. 17) shows complete loss of the shadow of bony articular cortex of the subastragalar joint. Cartilage space is present in approximately normal width.

Operation: Resection of subastragalar joint. Tuberculous granulations were found within

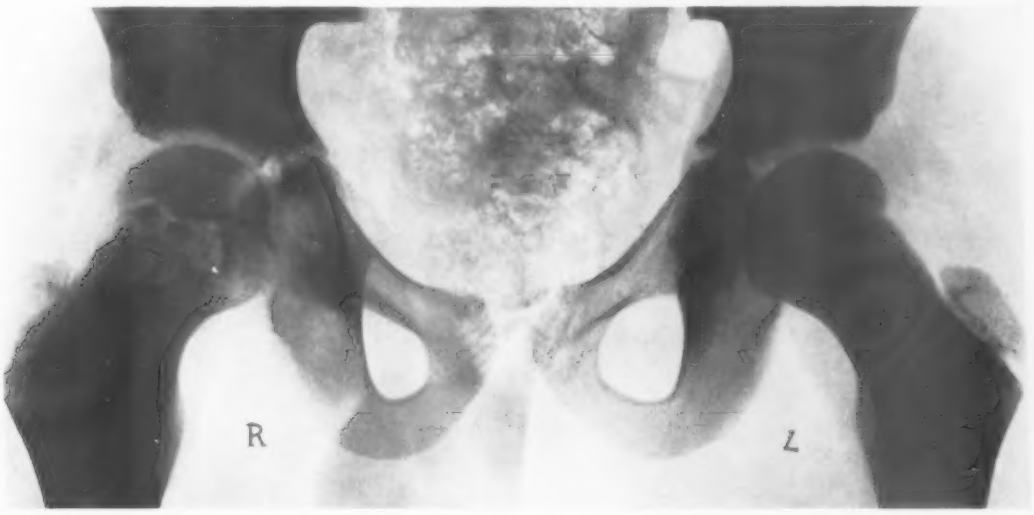

Fig. 16. Case vi. Primary metaphyseal bone lesion in tuberculosis of right hip. Roentgenogram shows regional atrophy, slight marginal loss of shadow of bony articular cortex of femoral head and an irregular area of reduced density in metaphysis, containing numerous smaller shadows of bone of normal density (sequestra).

may be less quickly accomplished than in adults because of its greater thickness in children. This is particularly true of the knee joint. Subchondral granulations rarely undermine and loosen the layers of cartilage at the knee, leaving them free in the joint as is often the case in adults. However, subchondral granulations may undermine and loosen the cartilage in other joints in which the layer of articular cartilage is proportionately thinner. In that case the roentgenographic appearance is much the same as is seen in adults, where there is loss of shadow of the bony articular cortex with preservation of cartilage space. This is illustrated by the following case:

the joint capsule. The articular cartilages (Fig. 18) were found loosened from the underlying bone by subchondral granulations but intact, and after severing peripheral adhesions were easily lifted out. Surface granulations were found only at the margins of the articular cartilages and destruction from this source had not taken place to any extent.

Secondary invasion of the bone at the weight-bearing points is seen also in children. It produces extensive necrosis but differs from that in adults in that the areas of involvement usually break down and are completely destroyed instead of remaining as sequestra. Whatever changes take place on one side of the joint also take place on

FIG. 17. Case VII. Tuberculosis of subastragalar joint. Roentgenogram shows regional bone atrophy, loss of shadow of bony articular cortex of subastragalar joint with preservation of its cartilage space. The other joints show normal shadows of articular cortex and cartilage space preserved.

FIG. 19. Case VIII. Tuberculosis of knee in child aged thirteen, showing laterally the opposing areas of destruction due to secondary bone invasion and medially the normal shadow of bony articular cortex and presence of cartilage space.

the other side, so that the invasion and destruction are usually bilateral.

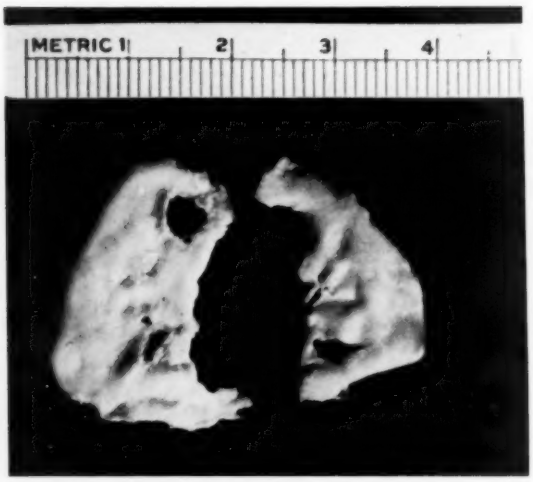

FIG. 18. Case VII. Photograph of detached articular cartilages removed at operation. Subchondral granulation tissue had destroyed bony cortex and detached cartilages from bone. Surface granulations were seen only at periphery of cartilage.

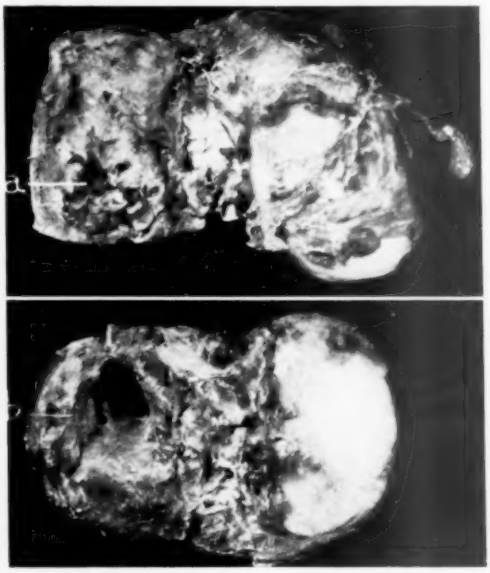

FIG. 20. Case VIII. Photograph of resected knee showing opposing areas of bone destruction of lateral half of femur (*a*) and tibia (*b*). Joint partitioned in midline by adhesions. Cartilage preserved in mesial half. Fibrous membrane covers most of medial condyle but is not attached to cartilage.

With equally advantageous treatment there is a greater tendency for healing to take place in tuberculous arthritis in children than in adults. There is more frequent partitioning of the mesial from the lateral portions of the joint in children. The disease may remain quiescent in one partition and recur in the other with resultant breaking down of articular surfaces and extensive destruction of underlying bone, while the other half of the joint shows relatively few changes. The following case illustrates these points:

Operation: Arthrodesis of knee joint. Figure 20 is a photograph of the resected joint. Dense fibrous tissue adhesions partitioned the lateral and medial joint compartments. On the lateral side there was extensive tuberculous synovitis and the articular cartilages of both lateral condyle and lateral tuberosity had been entirely destroyed. A large cavity containing caseous débris extended through the lateral condyle and the lateral portion of the epiphyseal cartilage plate. A similar though less extensive area of destruction was present in the opposing tibial tuberosity. The medial portion of the knee joint presented a much less advanced and apparently

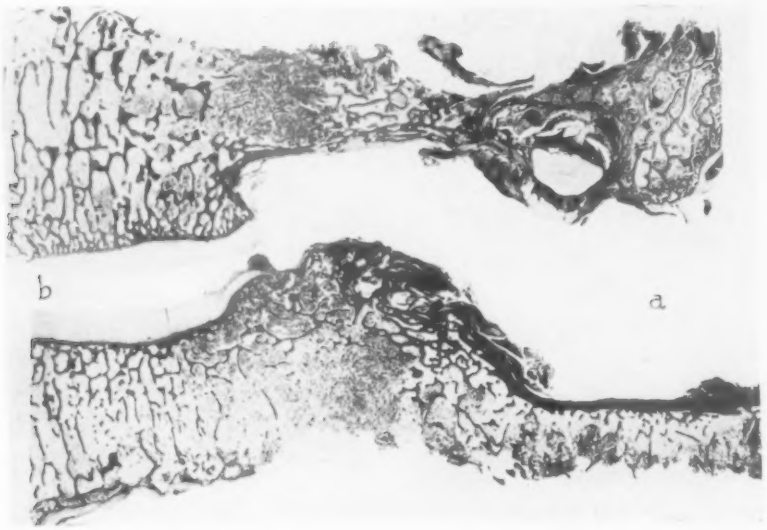

Fig. 21. Case VIII. Coronal microscopic sections through femur and tibia showing cartilage and bone destroyed laterally (*a*) and fairly well-preserved cartilage medially (*b*).

Case VIII. E.W., female, aged thirteen, had had intermittent pain and swelling of the right knee for ten years. During the last five years symptoms had been more severe, necessitating immobilization over long periods. At examination almost full range of motion was present, although somewhat painful. Valgus deformity at the knee was present. A roentgenogram (Fig. 19) shows opposing areas of bone destruction in the lateral femoral condyle and lateral tibial tuberosity. The destruction in the condyle has involved the epiphyseal cartilage plate and asymmetrical growth of the lower end of the femur has produced a valgus deformity. On the medial side of the joint the shadow of bony articular cortex is present and cartilage space is present though slightly narrowed.

arrested stage of the tuberculous process. The articular cartilages here were in a good state of preservation, surface destruction having taken place only at the periphery. A fibrous membrane unattached to articular cartilage covered the posterior half of the medial femoral condyle. Microscopic examination (Fig. 21) revealed an active tuberculous process on the lateral side of the joint, but on the medial side dense fibrous tissue containing only an occasional tubercle was found. Articular cartilage showed only marginal destruction in the region of the patella.

Secondary invasions of the bone have often been mistaken for primary osseous foci, but here again as in adults they may

usually be distinguished by the fact that both sides of the joint are invaded. In tuberculosis of the hip secondary invasions of the head of the femur and the iliac portion of the acetabulum are often seen, leading to breaking down of bone in opposing portions of the joint. This is illustrated by the following case:

CASE IX. C.G., female, aged eight had slight pain in the left hip for five years. During the last year the symptoms had become more severe. Examination revealed only slight restriction in motion at the joint. The roentgenogram (Fig. 22) shows moderate regional atrophy, cartilage space somewhat thinned but present, and shadow of bony articular cortex fairly well marked over the superior weight-bearing portion of the joint but poorly defined over the lower portions. Opposing areas of rarefaction are seen in ilium and femoral head.

Operation: Arthrodesis by means of tibial bone grafts. Tuberculous synovitis was present. Microscopic sections (Fig. 23) of cartilage and bone removed from superior portion of joint showed partial detachment of the cartilage by granulations composed of fibroblasts, macrophages, blood vessels and occasional foreign body giant cells. Sections of synovia showed typical tuberculous granulation tissue.

FIG. 22. Case IX. Tuberculosis of left hip in child of eight, showing opposing regions of bone destruction in acetabulum (*a*) and femoral head (*b*).

SUMMARY

Tuberculous arthritis may be primary either in the bone or in the synovia but there are no very reliable statistics as to the relative frequency of each. In either case a diffuse tuberculous synovitis eventually develops and the granulations attempt to spread over the surfaces of articular cartilage and destroy it. In some joints the articular cartilages fit accurately together while in others, particularly the knee, they are of different contour, so that there are large areas of both free and contacted surfaces. In joints with articular cartilages extensively in contact the granulations are kept off of the surfaces of the cartilage but destroy it to some extent by erosion at the margins. In joints with both free and contacted surfaces of cartilage the free cartilage is gradually overgrown and eroded by the granulations. As the disease progresses in all tuberculous joints the articular cartilage suffers from nutritional disturbances and from the action of tubercle toxins and subchondral granulations form, usually of a non-specific type and free from tubercles. They gradually absorb the bony articular cortex and deeper portions of cartilage and may eventually detach the cartilage completely. The loosened cartilage may persist for a long time because of the absence of proteolytic ferments in tuberculous exudate. At this stage the roentgen characteristics in joints with articular cartilages extensively in contact are: regional bone atrophy, reduction

or loss of density of the shadow of bony articular cortex, and preservation of the normal width of cartilage space of the joint. In joints, as the knee, with extensive areas of non-contacted cartilage the overgrowing surface granulations may destroy the entire thickness of cartilage and underlying bony cortex in a part or the whole of such areas before there is extensive development of subchondral granulations. The roentgen characteristics of such a joint are: regional bone atrophy, diminution or loss of the shadow of bony articular cortex in the non-contacted regions and preservation of the shadow of bony articular cortex and of the cartilage space in the contacted regions of condyles and tuberosities. Eventually the entire articular cartilages may be destroyed. This results roentgenologically in a narrowing or complete loss of the cartilage space of the joint.

In the advanced stages the bone may be secondarily invaded at the traumatized points of contact and weight bearing resulting in large areas of necrosis. The invasion is usually bilateral at opposite points in the bones and such areas after a long time may become detached resulting in kissing sequestra. The roentgen characteristics of areas of secondarily invaded and necrotic bone are a more or less conical or hemispherical shadow of bone bordering on the weight-bearing portion of the joint, with an incomplete line of demarcation about it and usually casting a denser shadow than the surrounding living bone. Usually the shadow of bony articular cortex of normal or reduced density is preserved on it and the condition is bilateral giving the picture of kissing sequestra. In some instances the dead bone is completely destroyed leaving pits or grooves along the joint surfaces.

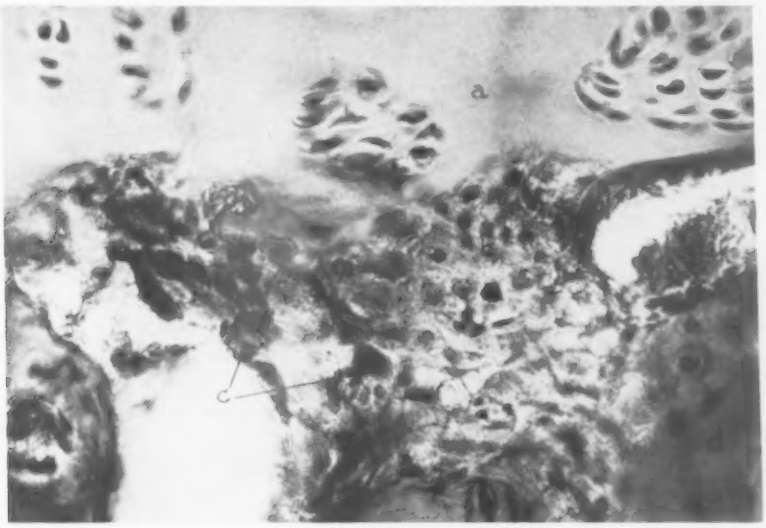

Fig. 23. Case IX. Microscopic section (×600) through superior portion of acetabulum. Shows articular cartilage (*a*), subchondral granulation tissue (*b*), consisting of fibroblasts, mononuclear cells and giant cell of foreign body type (*c*) and subchondral bone (*d*).

A primary focus in the bone bordering on the joint, if small, may break down leaving a pit or cavity. However, a large focus becomes separated as a sequestrum and retains its original density.

Tuberculous arthritis in young children varies somewhat in its pathology from that in adults. In the larger joints and in particular the knee, with relatively thick articular cartilages, destruction of the non-contacted portions by surface granulations is less complete than in adults. Also subchondral granulations do not frequently

detach articular cartilage leaving it free in the knee joint. In the smaller joints with thinner cartilages and in older children the course is more nearly like that in adults. Partitioning of the knee joint by healing processes occurs oftener and different degrees of involvement within the partitions are more pronounced in children. Primary bone lesions that can definitely be identified either by roentgen ray or at operation are more frequently located in the metaphysis than in the epiphysis. Secondary bone invasion is usually bilateral in the joint and most marked at the points of weight bearing, as in adults, but it usually results in destruction rather than sequestration of the necrotic bone regardless of the extent of the involved areas.*

* For discussion see page 795.

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ROENTGEN DIAGNOSIS OF BONE AND JOINT TUBERCULOSIS*

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IT IS perhaps no exaggeration to state that tuberculosis of the bones and joints is the most important disease with which the orthopedist is concerned and the economic and medical problem involved must be patent to even a casual observer. Aside from the dangers resulting from this process, the occurrence of a permanent deformity makes the proper understanding of its biology of paramount importance to every physician.

Current medical literature abounds in studies on tuberculosis of bones and joints. The number and excellence of these contributions attest to the intensive manner in which it is being studied. Many of the observations referred to attempt to classify this disease on a roentgen-pathologic or roentgen-anatomic basis. Numerous preferential localizations for it are enumerated and types are assembled under various headings or categories. While the proper understanding of any pathologic process is facilitated by a comprehensive classification, its object is often defeated by the complexity of a classification which is predicated upon minute variations in the disease picture. It may be that these efforts are well directed and that the ultimate product will represent a simple classification of an extremely complex picture. Essentially, however, morphologic and biologic variations are the field of the pathologist and if the roentgenologist is to take his proper place in the medical sphere of things, the recognition of this process becomes his most important function. Early diagnosis of the disease is an invaluable aid in reducing the ultimate disability and deformity.

The value of roentgen diagnosis in tuberculosis, while heretofore unquestioned by roentgenologists, has of late been seriously debated. This is illustrated by a recent statement that "there exists no roentgen picture that is entirely typical of joint tuberculosis in any of its stages." This assertion comes as a shock to those of us attached to orthopedic institutions and it was for this reason that I recently surveyed the clinical records and films of over 400 cases of bone and joint tuberculosis, many of which were followed for a period of eight years. The statistical result of this survey will be the subject of a future communication. At the present time, we are concerned only with the study of the diagnostic criteria utilized by roentgenologists particularly in the recognition of the early stages of the disease. It is my belief that tuberculosis can be recognized by roentgenologists fairly early and that the accuracy of the roentgen interpretation compares favorably with any of the diagnostic procedures commonly employed in medicine.

In the periodicals, insufficient emphasis has been placed on the early appearances of bone and joint tuberculosis, and the student must refer to his textbooks in order to familiarize himself with the changes produced by this disease. On the other hand, a study of the subject convinces me of the importance of revising radically our concept of the diagnostic importance of such alterations as were heretofore considered typical of this disease. My object will be to emphasize such alterations as are seen in the roentgenogram and upon which a diagnosis rests. One must understand, of course, that the interpretation of any disease does not depend upon a single finding but on a combination of signs or symptoms making up a complete picture. As an ex-

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ample, reference is commonly made in the literature to the typical atrophy of tuberculosis. The interpretation of any type of atrophy as specifically tuberculous is extremely hazardous and imparts to the term an importance which it does not merit. It is only the combination of this atrophy with associated phenomena that forms a picture which we recognize as tuberculosis.

The following alterations must be considered in the roentgen diagnosis of tuberculous joints: (1) synovitis; (2) soft tissue swelling; (3) bone atrophy; (4) bone sclerosis; (5) bone destruction; (6) bone production; (7) narrowing of the joint space; (8) sequestration; (9) cold abscess formation; (10) complications such as deformities, subluxations or sinuses.

SYNOVITIS

The first reaction of any joint to either trauma or disease is swelling of the synovial membrane and accumulation of fluid. Tuberculosis exhibits this phenomenon. It is important for the roentgenologist to remember that synovitis may recur frequently in derangement of the semilunar cartilages and in villous arthritis. In chronic nonspecific arthritis, the reaccumulation of fluid may indicate reactivation of the process. In these circumstances, the bone atrophy and synovitis produce on the roentgenogram an appearance almost identical with early tuberculosis. The presence, therefore, of an effusion does not specifically identify the process.

The size and extent of the effusion will vary with the severity and type of the infection as well as the size of the synovial sac involved. When large synovial sacs are freely distensible, as in the knee joint, fairly typical evidence of its presence is readily noted; whereas in the smaller joints, such as the wrist, hands and feet, this process may not be discernible.

The roentgen determination of an effusion is based on direct and indirect evidence. The direct evidence is a clouding of the joint space whereas the indirect evidence is the deformity of the soft parts due to the accumulation of fluid. So that in the study of early tuberculosis, clouding of the joint space may be the first indication of disease. In the knee joint, this may be evidenced by a distinct suprapatellar swelling which is greatest in synovial tuberculosis. So-called riding of the patella is but another evidence of the presence of fluid. In the ankle joint, the effusion extends along lines of least resistance and is characteristically noted as a protrusion posteriorly into the triangular space formed by the Achilles tendon, the superior surface of the os calcis and the posterior surface of the tibia.

In old lesions, the effusion is not present and its sudden recurrence in a joint is strong presumption of the reactivation of the infection. In caries sicca no effusion is demonstrated.

SOFT TISSUE SWELLING

For purposes of roentgenographic description, the soft tissue changes noted in this disease may be grouped into four classes:

1. The usual type of periarticular swelling noted in the joints, particularly of the long bones.
2. Soft tissue masses produced by involvement of the bursae.
3. Tuberculous infiltration of the soft structures.
4. Presence of cold abscesses.

Periarticular swelling due to inflammation of the periarticular tissues is frequent in tuberculosis. In long-standing cases, the persistence of this infiltration associated with atrophy of the muscles produces a fusiform deformity. The periarticular swelling or paravertebral soft tissue thickening that is seen in Pott's disease is of extreme importance in the early diagnosis of this lesion and may often be recognized even before actual destruction is present. Whether it represents active infection of the soft parts or else protrusion of the ligamentous structures by accumulated pus is of no moment. It may also occur, however, in fracture, osteochondritis and neo-

plasms of the spine, but in these instances the character of the associated changes in the segments often identifies the process.

Tuberculous bursitis is usually manifested roentgenologically as a massive localized swelling in the soft parts about the joint. Its character may be suspected when focal erosion occurs in the underlying bone or else where limited periostitis is noted. These swellings are commonly noted about the olecranon process and greater trochanter of the femur.

Tuberculous infiltration of the skin associated with changes in the subjacent bone occurs in sarcoid. Fusiform swellings result which are identical to those which occur in tuberculous dactylitis. The increase in the diameter of the extremity in sarcoid is due to the soft tissue infiltration and in tuberculous dactylitis to an actual increase in the width of the bone due to periosteal thickening, as well as the inflammatory reaction in the soft tissues about it. In the intercondylar region of the knee joint, a localized thickening of the soft tissues indicates a tuberculous pannus and identifies the lesion before destructive changes appear.

Synovitis and periarticular swelling occur in all the arthritides and, aside from the exceptions noted in the spine, its interpretation in the diagnosis of tuberculosis is of questionable value. Its association, however, with other alterations in the joint forms but an additional link in the diagnosis of an extremely complex picture.

Cold abscesses will be discussed separately under complications.

BONE ATROPHY

The subject of bone atrophy represents an unexplored field in medicine. Accurate differentiation has not as yet been made microscopically between the various types and degrees of this process. Roentgenologically, it must be considered as decalcification which is but a manifestation of resorption or destruction.

Bone atrophy may be produced by disease, disuse or metabolic dysfunction. One can state in a general way, therefore, that atrophy from disease occurs at the site of the pathologic process; that atrophy from disuse occurs in the entire member affected, and that atrophy from metabolic dysfunction is a universal process affecting all the bones of the skeleton. There is a certain degree of disuse in all articular disease so that atrophy is usually due to a combination of factors.

The production of bone atrophy in tuberculosis is probably due to many causes. The intense pain produced by the inflammatory process limits function of the part, so that it is immobilized. But pain and disuse occur in most of the arthritides, yet the decalcification is not so marked. The difference in the picture is probably dependent upon the nature of the infecting organism. It is conceivable that there is produced by the tubercle bacillus an osteolytic substance which acts on bone as an extremely toxic agent.

In early tuberculosis, the epiphysis of the long bones so affected may show this process. This atrophy has been referred to as "ground-glass," "washed out" or "egg-shell" type, etc. Its earliest stages may be represented as a simple loss of cancellous detail, or else a clouding or blurring of the trabecular structure so that individual striae appear denser than others.

In early cases, this decalcification may be completely absent, particularly in lesions of the spine and more particularly in lesions of the elbow and knee. In severe affections, on the other hand, or in old infections, the osteoporosis of the epiphysis, and to a lesser degree of the adjacent metaphysis, may be so extreme as to make good bone detail or definition impossible. In the subchondral region of the acetabulum, particularly in the region of the acetabular shelf, this alteration is extremely marked and appears as a crescent-shaped area of increased radiolucency, which may be the only manifestation of an early lesion in this area. So, also, a crescent-shaped area of osteoporosis beneath the articular surface of the glenoid fossa may represent an early

tuberculous process even before actual destruction occurs. In the knee this process occurs most commonly in the femoral epiphysis, particularly externally and posteriorly, whereas the tibial condyles, while they take part in the disease, appear to be affected later in the process. In tuberculous involvement of the ankle joint, a transverse area of decalcification occurs immediately above the articular surface of this segment frequently combined with an extreme osteoporosis of the astragalus. This atrophy may be fairly homogeneous in nature or else its continuity may be broken by extremely minute, multiple, punched out areas representing necrotic foci.

The extent and degree of this change may in a general way be an index to the severity of the disease. Extreme atrophy occurring early indicates a severe and active infection, whereas moderate atrophy occurring in long-standing disease may indicate an attenuated infection or transition from an active to a quiescent process. In para-articular or in synovial tuberculosis, the degree of atrophy appears to be of minor importance and seems to occur only, if at all, late in the disease. In some localizations such as in the phalanges of the hands and feet, atrophy is of no import and may be entirely absent.

BONE SCLEROSIS

The absence of bone atrophy by no means excludes a tuberculous infection. Sclerosis frequently occurs and should be listed as a change noted in this disease. It is important to remember that sclerosis may exist even in uncomplicated cases, and in some sites, such as the spine, it may be the predominating change. Whether it represents an avirulent infection or a stage in the development of the disease, combined with static phenomena, is for the roentgenologist of no very great moment. The view that sclerosis in the spine is produced by condensation of cancellous structure or destroyed bodies is erroneous, as has been pointed out by Freund,[1] since it is present in vertebrae of normal height. The point to be emphasized is that bone sclerosis occurs in tuberculosis even in the absence of mixed infection or surgical intervention. We are not referring in this instance to the pseudosclerosis produced by the silhouette of an overlying, partially calcified cold abscess. Some of our cases of Pott's disease of the spine which were followed for a period of three or four years never showed atrophy. It is interesting to note in this connection that the sclerosis in these cases may completely disappear following surgical intervention since such maneuver may transfer a low-grade infection into a fairly active and virulent process.

BONE DESTRUCTION

Bone destruction and bone production are the two fundamental piers upon which the whole structure of roentgen diagnosis rests. Familiarity with the localizations of these processes is the sine qua non of accurate interpretation.

The size of the lesion will be dependent, of course, upon the severity and duration of the disease. In early cases, loss of cancellous detail in articular cortex may be the earliest roentgen evidence of the process. On the other hand, extensive lesions involving the epiphysis and metaphysis, as well as articular cartilage, are already present on first examination.

As Phemister[2] states, evidence of destruction is usually seen at the edge of articular margins where destruction is produced by granulation tissue. It is usually found in the subchondral region, commonly in the epiphysis. Frequently in children it may be found in the metaphysis from which it extends into the joint, either directly through the epiphyseal cartilages or via the epiphysis proper.

In a general way, the destructive lesion may conform to several types. Occasionally these areas are of the infarct, wedge, or cone type, and are supposedly due to infarct of the vessels of the segment producing in the bone the phenomenon similarly noted in the lungs. They are wedge or

triangular in shape with the base directed towards the periphery of the part. We have noted this appearance frequently in the lesions of the epiphyses of the hip, knee and in the vertebra. On the other hand, the first indication of a destructive lesion may be a small, gouged out area, or moth-eaten zone, at the osteochondral junction of the metaphysis of long bones. At times localized abscess formation may be present either in the metaphysis or in the epiphysis. They simulate the common bone abscess except that they present, as a rule, no marked sclerotic border.

In the spine, extremely small areas of necrosis may occur in rapidly fatal cases and yet not be demonstrated roentgenographically. In this instance, the diagnosis is made on autopsy or on examination of the specimen. In this connection, it must be emphasized that the spinal cord may be constricted by granulation tissue, if it extends into the neural canal, and paralysis may be present with little roentgenographic evidence of the disease. Fortunately, however, the tuberculous process does not extend as much posteriorly as it does anteriorly. On the other hand, an entire body or several bodies may be destroyed and an extremely large hiatus exist between them, and neurologic symptoms may be absent. Skipped infections are extremely common. Here multiple involvement occurs in contiguous or distant vertebrae via the ligamentous structures, which by their propinquity, involve preferentially the anterior margins of the vertebrae and produce defects in the bodies similar to that noted in aneurysms. Extension of the lesion may also occur by direct continuity or through the blood stream. Commonly in the subchondral regions, the destructive process erodes the bone in an irregular saw-toothed manner. This type of lesion most frequently produces massive sequestra and destroys articular cartilage late in the disease.

BONE PRODUCTION

Although tuberculosis is essentially a bone-destroying disease, instances are encountered in which bone production is the dominant process. It is difficult to decide whether such cases represent a stage of the disease or a specific modification of it. That the productive type of tuberculosis occurs cannot be denied but that a specific type or strain of the tubercle bacillus is responsible for the lesion cannot be definitely proved.

One occasionally sees tuberculosis of the spine in children in whom the general picture seems to indicate a mild process. Constitutional reactions are slight, and the roentgenogram reveals an osteitis of a segment associated with slight compression; but no kyphosis, or abscess formation. In this instance the disease appears to be extremely mild and the local situation remains unaltered for a considerable time. If these patients are observed for a period of years, it will be found that the occurrence of an acute infection or a trivial injury radically changes the entire picture. The roentgenogram will then show changes in the segment which we recognize as a fairly active process.

We have seen diaphyseal tuberculosis in which the lesion on the roentgenogram resembled the sclerosing osteomyelitis of Garré and was diagnosed only on biopsy. We do not believe that this lesion can be correctly interpreted roentgenologically in the absence of alteration in the contiguous joint.

In tuberculous dactylitis, the destructive process is associated with a reactive periostitis which makes differentiation between it and luetic dactylitis extremely difficult and at times impossible. There is, however, a greater tendency towards bone production, sclerosis and periostitis in luetic dactylitis. A rarer type of dactylitis is that which is noted in sarcoid. This disease is a form of tuberculous dactylitis associated with changes in the skin. So that the occurrence of punched out areas in the phalanges associated with fusiform swellings of the soft tissues easily identifies this process. Enchondromata with which it may be confused are, as a rule, not associated with soft tissue swellings.

Up to within recent years the presence of hypertrophic changes in a joint was considered sufficient evidence to exclude a tuberculous infection; if present they were ascribed to mixed infection or other complications. This view is erroneous. Hypertrophic changes may occur in a joint in the absence of a sinus or mixed infection.

In the lumbar spine of adults, small bony spurs may extend from the anterior or lateral margins of contiguous bodies. They probably represent osteoperiosteal proliferations or calcification in the ligamentous structures. They seem to occur in those vertebrae where destructive changes are negligible and where narrowing of the joint space is a prominent feature of the disease. The cortical residue remaining after absorption of a neighboring tuberculous focus is not to be confused with this phenomenon. It is our opinion that these processes represent an attempt at repair, although it is possible, as has been pointed out in the German literature, that they are, evidence of a severe static disturbance that leads to a marked degree of tuberculous spondylitis.

Marginal hypertrophic changes are extremely common in tuberculosis of the hip as evidenced by bone production about the rim of the acetabulum as well as the margins about the head of the femur. This process of bone production may also occasionally be seen in lesions in the knee where osteophytic protrusions extend from the condyles of the tibia or else where calcification of the ligaments or tendons herald nature's efforts to splint the part.

Local or remote periostitis may also occur in the absence of a sinus. Although often referred to as a primary tuberculous osteoperiostitis, it has been our conception that they are extensions of an infection from a neighboring joint. In the smaller bones of the hands and feet, parallel periostitis may exist and bone production may be present without any evidence whatever of necrosis of the underlying shaft. It is impossible roentgenographically to distinguish these cases from luetic dactylitis. Periostitis is extremely common in lesions of the ankle joint. In the elbow joint, curiously enough, "lace-work" periostitis occurs and the differentiation between tuberculosis and gumma is almost impossible.

NARROWING OF JOINT SPACE

Contrary to accepted belief, narowing of the joint space is not a characteristic feature of early tuberculosis. Actually if it occurs it comes late in the disease, with certain exceptions. Its existence is dependent essentially on the localization and duration of the destructive process, rather than as a special feature of the lesion. While destruction of articular cartilage is present in tuberculosis, the greater force of the destructive impulse is expended on articular cortex. In other words, bone is destroyed before cartilage, so that even in long-standing cases, the joint space is relatively unimpaired.

The width of the joint is maintained by detached segments of cartilage and granulation tissue and as Phemister[2] has indicated, the persistence of these cartilaginous discs is due to the absence of the proteolytic ferments which are present in pyogenic infections. Thus, digestion of the discs does not occur in tuberculosis.

In seeking the causes for the relative integrity of the joint space, one must also bear in mind that the destructive granulations erode the bone at the margins of cartilaginous attachments and that the main force of the destructive lesion may assert itself at points relatively remote from weight-bearing surfaces. This is particularly true of the larger joints such as the knee and hip. The lesions in the knee may involve the condyles of the femur posteriorly or the intracondylar region anteriorly—where no weight-bearing is present and consequently no change in the width of the joint results. Again, fairly large necrotic areas may be present at the lateral margins of the epiphysis and metaphysis with no narrowing of the joint space. Often the converse happens; the collapse of the involved bone such as a vertebra may actually result in an increase in the width of the

intervertebral spaces. In the margins of the acetabulum, small necrotic foci may exist as subchondral abscesses or else invasion of the bone may be indicated by sequestra, but the width of the articulation remains unaltered.

There are, however, several exceptions to this observation. In the intervertebral articular type of tuberculosis narrowing of the joint space is one of the early roentgen evidences of the disease. Here osteochondral erosion often exists and is not visualized roentgenographically. We have seen this process in the dorsal spine associated with a fairly large abscess but the body of the vertebra was unaltered. In infections of the wrist or elbow joints, narrowing of the joint space may occur early and is probably due to rapid destruction of rather thin articular cartilage, by a virulent infection.

In old cases, narrowing of the joint space is present and is but a manifestation of destruction of articular cartilage. However, even in old lesions it may still be possible to delineate the joint line, even where mixed infection has produced bony ankylosis.

In pyogenic infections, destruction of articular cartilage results in early obliteration of the joint space. This fact is of the utmost significance to the roentgenologist. His interpretation of the roentgenogram resolves itself into an intelligent appraisal or estimate of the duration of the infection and its effect on the joint space or, conversely, whether the damage to the joint cartilage has occurred either early or late in the infection. Complete obliteration of a joint which has occurred in three or four weeks is rarely tuberculous and if the roentgenologist bears this fact in mind it will prove an invaluable aid in diagnosis.

SEQUESTRATION

The presence of a sequestrum in tuberculosis is an indication of involvement of the subchondral bone. Tuberculous granulations burrowing under the cartilage and invading the osseous structure separate fragments of bone, which exhibit great variability in size and number depending on the severity of the destructive process. In the bones about the larger joints separation is facilitated by pressure and movement of the part; whereas the process is somewhat impeded in the shafts of the small tubular bones and in the vertebrae. When these fragments occur on both sides of the joint, they have been termed "kissing" sequestra. Due to the fact that the cartilaginous covering is not visualized, sequestra appear smaller than they actually are.

Sequestra usually appear denser than the bone from which they have been detached. In this instance, what appears to be sclerosis actually represents a distinct fragment of bone in the locale of an osteoporotic area. The density of these fragments moreover appears to be dependent upon two factors: (1) it represents the absence of resorption in a bone whose circulation has been interrupted and (2) the osteitis of a loose fragment produced by friction or abrasion of neighboring movable parts. In general, however, the sclerosis of the fragment is more apparent than real since it is present in or about bones that are atrophied from disease or disuse.

The density of the fragment may be transitory in character and the eburnation may give way to atrophy in either of two instances. The small body may be absorbed or mixed infection precipitate further necrosis and the sequestrum in this instance may be completely destroyed or extruded.

The presence of a sequestrum is, as a rule, readily recognized but it may exist and not be demonstrated roentgenographically. The explanation for this lies in the fact that the limiting osteoporotic border is not sufficiently marked to be visualized or that the severity of the infection has not as yet produced relative inequalities in the density of the affected member. Occasionally, however, the sequestrum may be unexpectedly discovered by the presence of a localized circular border of decreased density. This border may mark the crater in

the bone remaining after the detachment of the free fragment. Fortunately, however, the line of demarcation between necrotic and normal bone is so frequently present as to make accurate interpretation relatively simple.

COLD ABSCESS

The most common complication of tuberculosis is the formation of a cold abscess and its recognition is extremely important, since it indicates the character of the lesion.

The location and migration of an abscess is perhaps influenced by two factors: the consistency of the mass and the presence of soft tissue barriers preventing the extension of the process to other levels. When small they are usually confined by the capsule of the joint but as the volume of the detritus increases, they perforate the capsule and appear on the free surface of the skin, or extend to other levels. The shape of the shadow is somewhat determined by the pressure of surrounding structures, particularly where the main mass of the fluid has gravitated to other areas. Thus, they commonly assume fusiform, globular or saccular shapes. At times irregular dissecting opacities may be demonstrated in the soft parts. The density of the shadow is dependent upon the degree of calcification in the mass which is but an indication of nature's effort to cure.

It is important, moreover, to remember that an abscess may be demonstrated where there is but slight involvement of the joint and, conversely, that destruction of osseous structure may exist without abscess formation.

There are several peculiarities of abscesses of the spine. In the cervical region, retropharyngeal abscesses occur and are recognized readily by the forward protrusion of the pharynx. At times, however, they point in the lateral angles of the neck. In the dorsal region, small paravertebral densities located about one or more bodies usually assume a globular shape. Before much necrosis is visualized, the presence of an abscess in the dorsal region can often be inferred by the apparent dissimilarity in the density of the segment when seen on the anteroposterior and on the lateral roentgenograms. When an osteitis of a body is noted on the lateral view, and no change in density of the same segment appears on the anteroposterior view, the probabilities are that a small abscess exists. The explanation for it is that the minute variation in the density of the segment produced by the mass is visualized better in the lateral view, since the abscess is usually situated laterally.

According to Freund,[1] extension of a paravertebral density equally above and below a necrotic area may indicate that its greatest mass consists of granulation tissue; whereas the formation of large fusiform or saccular shadows probably indicates the preponderance of seropurulent material. Large dorsal abscesses may be arrested at the level of the diaphragm where they produce extremely broad saccular opacities. Although limited as a rule by the ligamentous attachments of the diaphragm, in extreme cases extension of these abscesses into the abdomen may occur.

Disappearance of an abscess may occur under certain conditions. The abscess may either be absorbed or calcified. Sudden disappearance of an abscess usually indicates perforation through soft tissue barriers and extension to other levels. Large abscesses whose existence may have been unsuspected often are clearly demonstrated following stabilizing operations and, on the other hand, rapid extension of an existing abscess frequently follows such maneuver.

In the lumbar region, the earliest indication of an abscess may be an outward bulge in the shadow of the psoas muscle. In any destructive lesion of the spine, particularly in the lumbar region, this deformity of the psoas indicates an abscess and should be interpretated as such even in the absence of flocculent calcific deposits.

Abscesses produced by involvement of the sacroiliac joint usually perforate into the pelvis through the weak anterior portion of the capsule or posteriorly through

the buttocks and in extreme cases may extend into the upper portion of the thigh. Stereoscopic plates of the pelvis will often demonstrate a soft tissue density in the pelvis corresponding to the mass.

It is probable that the more universal employment of high speed roentgenography may permit earlier recognition of abscesses about the hip and knee joints.

SINUS FORMATION

When tuberculosis is complicated by the formation of a sinus, it loses its identity so far as the roentgenologist is concerned. The mixed infection that inevitably supervenes destroys whatever individuality the lesion may have possessed. The changes of an osteomyelitis or a pyarthrosis dominate the picture.

As I have already indicated, roentgenologists are thoroughly aware of the secondary changes that occur in tuberculosis following mixed infection. It is necessary only to call attention to the fact that proliferative changes may be absent even where mixed infection exists.

For surgical reasons the roentgenologist is frequently requested to determine the origin of sinus tracts, particularly when they occur in the buttocks or upper third of the thighs. The use of lipiodol frequently yields a surprising amount of information regarding the size, shape, extent and point of origin of these tracts. Stereoscopic plates taken after lipiodol injection may trace the course of a sinus to an extremely small erosion whose presence may have been unsuspected and whose character was not positively identified.

DEFORMITIES AND SUBLUXATIONS

Due to the destruction of articular surfaces and the forces exerted by muscular traction and by the weight of superimposed parts, deformities and subluxations are of frequent occurrence in this disease.

The gibbus produced by a scrofulous lesion in the spine is a familiar phenomenon. Since the roentgenologist utilizes this deformity as an aid in diagnosis, several features of this process may properly be emphasized here. In typical Pott's disease, destruction of one or more vertebral segments may exist without the production of a gibbus whereas, on the other hand, destruction of a single body may result in a fairly marked kyphosis. The institution of corrective measures early in the development of the lesion as a rule limits the deformity. We have seen the kyphosis progress, however, even after the application of immobilizing devices, and fusion operations. Bone grafts inserted in the spine for fusion purposes will readily unite to the arches and spinous processes but may themselves acquire a bowing deformity as great as the original kyphosis.

In advanced tuberculosis of the spine, the kyphosis may either be marked or surprisingly slight considering the extent of the destructive process. Autopsy specimens sometimes reveal ankylosis of the articular facets at or about the site of the lesion resulting in spontaneous fusion preventing extension of the deformity.

Upward and inward migration of the acetabulum and femur is commonly seen. Outward migration of the femur occurs more frequently in pyarthrosis. Acute luxations in general are more frequent in pyarthrosis than in tuberculosis.

At the knee joint, posterior subluxation of the tibia is almost the rule but anterior luxations of this bone may occur.

At the elbow joint, in advanced cases posterior subluxation of the radius and ulna may occur.

SUMMARY AND CONCLUSIONS

From what has already been said, it seems obvious that criteria utilized in the roentgen diagnosis of tuberculosis are subject to diversified exceptions which make accurate interpretation of this disease extremely difficult. The changes in the bones and joints are dependent upon the severity and duration of the process as well as the specific locality involved. The presence of a sinus and infection introduces factors whose rôles in the process are extremely

difficult to evaluate. The intelligent appraisal of characteristic changes and the modifications produced by extraneous circumstances determine the successful diagnosis of the disease.

The usual roentgen changes of joint tuberculosis are as follows: synovitis and periarticular swelling, bone atrophy or sclerosis, bone production and destruction in epiphysis and metaphysis, narrowing of joint space, sequestration and the presence of cold abscesses or sinuses.

In the genesis of a tuberculous arthritis, most or all of these changes are present. The roentgenogram is but a record of the disease at a given moment.

1. Synovitis, periarticular swelling and bone atrophy are common to all arthritides and are only of corroborative value in the diagnosis of tuberculous arthritis. Bone atrophy is usually marked but its intensity is modified by numerous imponderable factors which complicate diagnosis.

2. Sclerosis and bone production occur in tuberculosis even in the absence of a mixed infection. Where sinuses exist, bone production may be absent. Diaphyseal tuberculosis in long tubular bones is rare and roentgenologically the diagnosis is impossible.

3. Wedge or cone-shaped lesions are usually tuberculous.

4. "Kissing" sequestra are common in tuberculosis.

5. Narrowing of a joint space which occurs late in an infection, despite associated destructive changes, is strong presumption of the existence of tuberculosis.

6. Complications such as kyphosis, subluxation, and sinus formation, occur in tuberculosis as well as in other arthritides.

7. Roentgenologically the presence of a cold abscess specifically identifies the process as tuberculous.*

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* For discussion see page 795.

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OSTEOCHONDRITIS, FOCAL AND MULTIPLE*

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INTEREST in the disease entity known as osteochondritis was initiated principally through the aid of the roentgen ray. Without the roentgen ray, its advent into the category of a recognized disease might well have been delayed many years. In 1903, shortly after the application of the roentgen ray to investigation of disease, a paper by Osgood, concerning the tubercle of the tibia, was the first attempt to describe a non-traumatic type of epiphyseal disease. In 1908 Köhler described the same process in the tarsal scaphoid and patella. Legg, Calvé, and Perthes, in 1910, independently reported changes in the capital epiphysis of the femur, while Sever in 1912 directed attention to the same process in the os calcis. It then remained for Freiberg, in 1914, to report the disease in the head of the second metatarsal. Scheuermann in 1921 recognized such a change in the secondary center of ossification of the vertebra, while Calvé in 1925 noted a similar change in the primary center.

Gradually it became apparent that all these conditions, known by the names of the authors describing them, were very closely related. The custom of applying authors' names to the disease, rather than thinking of it as a pathological entity which might involve any growing ossification center, undoubtedly masked for a long time the fact that all these lesions were the same process showing similar characteristics in their onset and progress. Thus, the disease entity, osteochondritis, was but slowly recognized.

The literature upon this subject is considerable, as evidenced by a complete bibliography published in a paper by Zollinger and myself[1] in 1930. The literature is also most confusing owing to the multiplicity of terms used to describe the same type of pathological change in the various ossification centers of the body. This led to a search for a classification and terminology which might be applied to the disease in its various skeletal foci. It seemed logical, therefore, to make the terms descriptive, designating the growth center involved and whether primary or secondary, and to combine in the term the fact that the process involved both cartilage and bone structures. With a paucity of pathological material and at present with a complete lack of knowledge of etiology, most important facts were lacking to arrive at a satisfactory nomenclature. When we proposed the term osteochondritis of growth centers, we were cognizant of the great doubt regarding the inflammatory nature of the disease. Subsequent pathological studies have served greatly to increase this doubt.

The etiology still remains obscure, even though there have been many attempts to produce the disease experimentally. Infection was originally thought to be responsible in some cases as evidenced by several investigators who recovered organisms from growth centers explored.

In one patient where the hip was explored and tissue for biopsy taken we were able to grow *Staphylococcus albus* aerobically and anaerobically. The clinical and pathological picture in this case was similar to several others which gave negative cultures.

A disturbance in blood supply, resulting from trauma to a growth center, has seemed likely in many instances, but this is not consistent with the histologic picture which we have seen since. In the majority of cases there has seemed to be an increased blood supply. Neither would this theory seem to account for its appearance in several members of the same family or for a generalized type of osteochondritis

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involving all of the major growth centers in a single patient. Heredity is suggested by the report of Hanson who observed the vertebral type in a child, parent, and grandparent.

Recently Schmorl has drawn attention to the "nucleus pulposus." He feels that the osteochondritis of the primary centers of ossification of the spine results from a disturbance in the development of the intervertebral discs. He terms this disturbance "kyphosis adolescentium." He observed a bursting out of the intervertebral plate in its pure form only in small children but seldom found it in the second period of development. He states that such asymmetries cannot be regarded as pathological phenomena, but only deviations of development within the normal physiological limits, and that they assume a pathological character only from the effect of overloading.

It is entirely possible that there are different types of this disease which we at present have not clearly recognized and that there may be several different etiological factors. In substantiation of this we have in a previous paper[1] demonstrated the disturbance in three members of the same family and in a paper[2] to be published have shown a patient with all the major growth centers involved with the process we term osteochondritis. Further, there is no constancy in the clinical picture of those patients with only one growth center involved.

Further study has convinced us that the variation in description of pathological material by different authors may simply mean that specimens for study have been removed during different stages of the disease, resulting in a varied picture which, if viewed with sufficient perspective, may allow us to gain a clearer conception of the pathology. We have reason to think that years are necessary for healing to take place in this disease, and that alone would seem to account for a great part in the variation of the histopathology.

The histologic examination of tissue removed from several children with primary osteochondritis of the upper femur showed a striking alteration in both the articular and epiphyseal cartilage. There was irregularity and density of the bony head which was thought to be due to the irregular retardation of enchondral ossification and to the production of osteoid rather than bone. Asymmetry and non-development of the head existed and it seemed that it might be accounted for as a failure in new bone formation, rather than as a destruction of already formed bone, inasmuch as the former was seen to be true, while there was no necrosis or unusual osteoclasis to indicate the latter. This lack of ossification was related to, if not caused by, a deterioration of cartilage, which was focal and ranged from simple fibrillation to necrosis of cells and dissolution of matrix. The cause of the cartilaginous degeneration was not apparent, although faulty nutrition was obviously suggested. Microscopic evidence of inflammation was not seen in either bone or cartilage.

In the several patients where biopsy was carried out, the cartilage was damaged to the extent of being unsuitable for enchondral ossification; it is, therefore, not difficult to consider the same process becoming extended to include the bone and cause the necrosis described by other authors.

In order to complete the pathological picture, the entire pathogenesis must be seen and studied. This can be accomplished if complete clinical and laboratory study of all cases is made by a biopsy according to the "Key block method."[2] It will then be possible to correlate pathological change with the gross and roentgenological appearance.

During the period before this disease was established as a definite entity, many of these patients were considered to have a tuberculous joint disease. Fortunately, with the aid of the roentgen ray this mistake is rarely made nowadays.

The variation in the clinical picture has previously been mentioned but needs

further elucidation, since the treatment necessarily is dependent upon this difference. In many children with osteochondritis of the hip the disease runs a rather mild course with a minimum change in the architecture of the epiphysis. These patients require little in the way of protection, but in our experience we have seen a large number of patients, particularly boys, where there has been considerable muscle spasm and even "night cries" with much malacia of the capital epiphysis. These have required prolonged periods of avoidance of weight bearing in order to prevent discomfort and at the same time to minimize damage to the soft epiphysis resulting from the thrust of weight bearing, and also to reduce the degree of deformity of the part. The same is true of the spine, and the insistence upon carrying out treatment is more difficult here because of the tendency of this process to be associated with very little pain. In contrast to the hip we have found the disease of the spine to occur more frequently in girls. Here the problem is largely one of preventing deformity; this can be done only by a prolonged period of recumbency upon a hyperextended frame in conjunction with hyperextension exercises, to be followed by a supportive type of brace until ossification of the centers is sufficient to prevent wedging of the bodies by the superincumbent weight of the body.

SUMMARY

A brief review of the history of the disease, osteochondritis, has been presented, emphasizing the need of a uniform terminology, but at the same time citing reasons why such is difficult in view of the lack of information as to etiology and of the paucity of pathological material from which to draw conclusions.

The etiological factor remains unsolved. In view of the fact that it may occur in single growth centers, multiple centers in the same patient, or in several members of the same family, it is probable that more than one etiological agent may be responsible.

Reference is made to a family in which three members presented the disease in the spine and also a patient in whom all the major growth centers showed the changes characteristic of osteochondritis.

The pathology of the disease is briefly discussed, suggesting that the variations in the histopathological picture presented by various authors may result from the fact that the specimens were removed in the several cases during different periods of the disease and that at a given stage the process may be the same.*

* For discussion see page 795.

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ROENTGEN FINDINGS IN CHRONIC POLYARTICULAR ARTHRITIS*

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THERE is perhaps no subject in modern medicine concerning which more has been written and less has been agreed upon than the classification of arthritis. Much of the confusion which attends this subject is due to a lack of exact knowledge of the etiology of the various forms of arthritis and to the paucity of careful studies on the pathology of this disease.

In a recent paper, Shapiro[10] clarifies the terminology to some extent in that he correlates the clinical, roentgenological and pathological classifications. He points out that the terms "rheumatoid," "atrophic," and "proliferative," when applied to chronic arthritis, probably refer to the same general type. Correspondingly the terms "osteoarthritis," "hypertrophic," and "degenerative" are practically synonymous in a broad classification. Shapiro advocates the use of a descriptive classification until a more exact knowledge of the etiology is at hand.

In the roentgen literature on arthritis there is a tendency to divide arthritics into three groups: atrophic, hypertrophic, and infectious. This classification, no doubt, originated with Goldthwait[5] and has been popularized among roentgenologists by Baetjer and Waters.[2] We find this usage in the latest edition of Holmes and Ruggles,[6] in fairly recent papers by Moore,[7] Vrtiak and Jordan,[11] and in many other publications. This grouping is open to severe criticism, as expressed by Shapiro, first because of the use of the term "infectious." In view of the prevailing opinion among the majority of investigators that atrophic or proliferative or rheumatoid arthritis is infectious in origin and of many that hypertrophic arthritis is also infectious in nature, the use of this term for a third division is unfortunate in that it implies that the other two are not infectious. It should be pointed out that Baetjer and Waters attempt to convey the impression of specific and nonspecific infections as distinguishing these groups, but the term as generally used is confusing.

The second criticism is based upon the studies of Nichols and Richardson[8] on the pathology of arthritis which have been largely confirmed and elaborated by Allison and Ghormley.[1] They found it impossible to distinguish grossly or microscopically, in almost all specimens, between those joints which were affected by a known bacterium, such as the gonococcus, and those in which the etiological agent was unknown. They found a proliferative process in either case. They found also that the distinction between the proliferative (atrophic) and degenerative (hypertrophic) forms was not always distinct and they gave no ground for the separation of a third group. In this regard it is of interest to note that Scott[9] in a recent paper divides his cases of arthritis into rheumatoid (atrophic) and osteoarthritis (hypertrophic) but subdivides the latter into infectious and non-infectious types.

As a further criticism of the whole classification there appears the recent work of Wetherby and Clawson[12] who found streptococci in the blood cultures of 50 per cent of a series of chronic arthritics which included cases of all three roentgenological types. They are impressed with the fact that 30 per cent of all their cases of chronic arthritis show rheumatic nodules[3] from which streptococci can easily be cultured. Among these also there are a number of cases which show the roentgen signs of hypertrophic arthritis while the majority belong to the atrophic group. The experience of Wetherby and Clawson[13] with

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intravenous streptococcic vaccination tends further to suggest that the majority of cases of arthritis are infectious in origin.

Casual observation of a large group of arthritics in whom roentgen examination of some of the painful or affected joints was made revealed the fact that they are usually polyarticular and that in some cases, at least, various joints showed very different roentgenologic findings. It was also noted that the history of the disease process might be much the same in two joints while the roentgen picture might be radically different. It was the contention of the clinicians[10] that the roentgenological distinction between atrophic arthritis and infectious arthritis was arbitrary and not consistent with the clinical picture. We therefore determined to investigate a series of cases with a view to making roentgenograms of all the joints which were then, or had ever been, affected by the disease process. Records were kept as to the age of the patient and the duration of the affection in each joint. For the purposes of this study the joints of each hand and each foot were considered as one. The spine was subdivided into cervical, thoracic, lumbar, and two sacroiliac joints. Miscellaneous joints included the acromioclavicular, sternoclavicular, and temporomandibular articulations. Sixty such cases were examined and in these, 564 joints, or an average of 9.4 joints per case, were roentgenographed. On the basis of both the clinical and roentgen findings, to the best of our ability, such conditions as gout, tuberculosis, syphilis, neuropathies, severe trauma, hemophilia, and other non-arthritic conditions were excluded.

The films of these joints were studied to determine the presence or absence of soft tissue swelling or atrophy, fluid in the joint, bone atrophy, eburnation of bone, cartilaginous destruction, bone destruction, new bone formation or calcification, bony ankylosis, deformity, or combinations of these findings. In studying any large group of chronic arthritics, any or all of these changes may be observed in many of the joints but many will be found to show no abnormal features whatever. The description of the roentgen appearance of these changes has been given so frequently in various textbooks and publications that it seems unnecessary to review them here. Certain combinations of these findings tend to stand out. In some cases can be observed soft tissue swelling associated with haziness of the joint, floating upward of the patella, filling out of the suprapatellar bursa, or obliteration of the posterior fat triangle of the ankle, indicating fluid in the joint. In others the combination of soft tissue atrophy, bone atrophy or decalcification, and destruction of cartilage as shown by approximation of the articular surfaces, is present. In another type there is added to the above findings punched out or irregular erosions of the articular surfaces. In other cases there is shown eburnation or increased density of bone and new bone formation in the form of spicules along the margins of the joint. To this may be added, in some cases, calcifications extending anywhere within the limits of the joint capsule and into the associated tendons. In still another group can be seen marked bone destruction of irregular character combined with approximation of the joint surfaces indicating cartilaginous absorption, and marked new bone formation. The latter may extend across the joint surface, as well as around the margins, and bony ankylosis may occasionally be seen.

Using these findings as a guide an attempt was made to classify all the joints into four groups: normal, atrophic, hypertrophic, and infectious. It seems desirable to indicate what criteria were used in placing joints in any one of the latter three divisions. We considered as atrophic arthritis (Fig. 1) those cases which showed soft tissue atrophy, bone atrophy, cartilaginous destruction, bone destruction, fibrous ankylosis, or various combinations of these as indicated in the preceding paragraph. Punched out erosions of the ends of the bones resembling gout, especially seen in the fingers and toes, were put into

FIG. 1. Atrophic arthritis. Anteroposterior roentgenograms of hand showing soft tissue swelling about joints, marked bone atrophy, cartilaginous absorption, some bone destruction, little or no bone production. Note involvement of practically all joints of wrist and hand. Note particularly marked bone destruction at second metacarpo-phalangeal joint without bone production.

this class. No cases with any appreciable degree of new bone formation were held to belong to this group. We considered as hypertrophic arthritis (Fig 2) those cases in which there was no bone atrophy or possibly some eburnation of the ends of the bones, relatively little cartilaginous destruction, little or no bone destruction, some bone production in small or large amounts. The new bone must appear in the form of spurs about the margins of the joint, calcification of the capsule or other joint tissues, or spurs extending into the tendons, but without any bony ankylosis. Finally in the infectious group (Fig. 3) were placed those cases in which there was marked bone and cartilaginous destruction together with new bone formation with or without ankylosis. This new bone formation tends to bridge across the joint. While these latter cases appear to be mixed types they were distinguished from the atrophic group by the presence of new bone formation and from the hypertrophic group by the presence of the marked cartilaginous and bony destruction and by the character of the new bone formation. Certain cases of chronic gonorrheal arthritis, for example, give this appearance in typical form. Nichols and Richardson describe certain joints as having these characteristics pathologically but they found proliferation of the synovial membrane in these and therefore did not distinguish them from the other proliferative (atrophic) cases.

Particular attention must be given to the spine in any such study. We considered the

FIG. 2. Hypertrophic arthritis. Lateral roentgenogram of knee showing moderate eburnation of bones, bone production around margins of patella, tibia, and condyles of femur. (Fabella is also present.) There is little or no bone destruction and only a moderate cartilaginous absorption. There is no bony ankylosis

cases of ankylosing spondylitis (Marie-Strümpell, Bechterew, rhizomelic spondylitis, etc.) to belong to the infectious group because of the ankylosing character of the new bone formation and the destruction of arbitrary but correspond fairly well to the descriptions found in the roentgen literature. For the purposes of this study the term "infectious" is used to designate a particular group of joints rather than as an

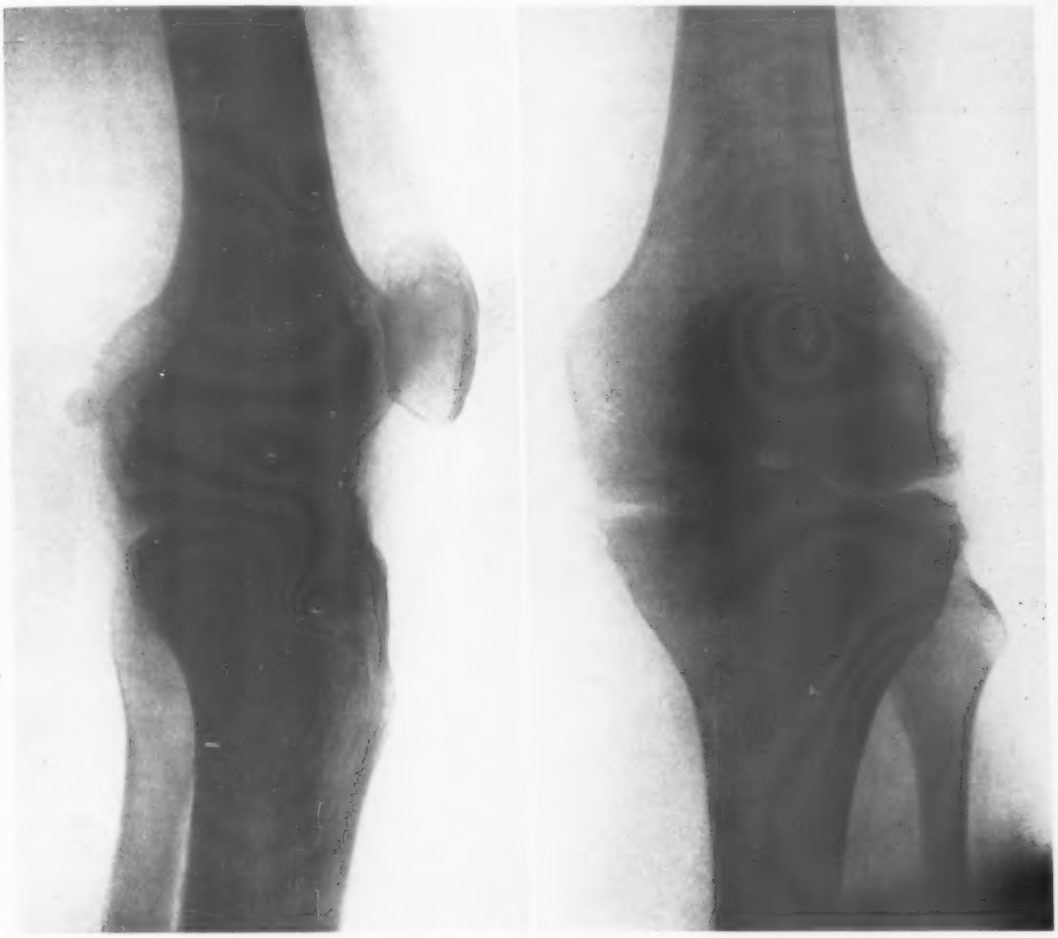

Fig. 3. "Infectious" arthritis. Posteroanterior and lateral roentgenograms of the knee joint in a case of gonorrheal arthritis. These show absorption of cartilage, marked bone destruction, and marked new bone formation bridging across the joints as well as around the margins. Note involvement of inner surface of patella (lateral view) and tendency toward bony ankylosis (posteroanterior view). (Fabella is shown in lateral view.)

the transverse articulations. The commonly seen spine with spurs, lipping, but little bone or cartilage destruction and no ankylosis was placed in the hypertrophic group. Only a few cases could be recognized as atrophic or destructive without new bone formation.

These divisions are no doubt somewhat indication of the etiology of any of the groups.

Of the 564 joints studied (Table 1), 25.3 per cent were classified as normal. This seems a very high percentage and may be accounted for in part by the manner in which the material was obtained. Any joint in which the patient had definite pain

TABLE I

SUMMARY OF CLASSIFICATION

Cases examined..... 60
Joints examined.....564
Average number per case..... 9.4

Percentages of Total

Normal Joint	Atrophic Arthritis	Hypertrophic Arthritis	Infectious Arthritis
25.3	31.4	23.2	20.1

or deformity or had had pain or deformity in the past was considered arthritic. No doubt some of these pains were referred from other joints while in some cases the process may have been of an entirely different nature. In some cases, no doubt, enough time had elapsed since the active process had been present for the joint to repair itself sufficiently to appear normal in the roentgenogram. Nevertheless it seems reasonable to conclude that a very large number of arthritic joints give no abnormal roentgen findings. This is probably due to the fact that chronic arthritis in its early stages and frequently throughout the disease, affects only the soft tissues of the joint which are not visualized in the roentgenogram.

The atrophic group comprised 31.4 per cent of the whole group, the hypertrophic 23.2 per cent and the infectious 20.1 per cent. The predominance of the atrophic group is consistent with the usual experience.

In Table II is given the percentage frequency of the joints involved, as shown in the first column. The succeeding columns indicate the frequency with which each type of involvement affected each particular joint. The miscellaneous group was so small in number that they are not considered, and the three spinal divisions were consolidated under one heading. The knee, hand, spine, ankle, and foot are the most commonly afflicted joints. It is notable that the hands show a markedly lower percentage of normals than do any of the other joints. This may be related to the fact that the hands are frequently the first joints affected and often the most severely damaged.

TABLE II

SPECIFIC JOINT RELATIVE TO TYPE OF INVOLVEMENT

Joint	Percentage of Total	Percentage of Normal	Percentage of Atrophic	Percentage of Hypertrophic	Percentage of Infectious
Foot.....	9.2	20	50	7	23
Ankle.....	10.3	38	33	7	22
Knee.....	16.5	20	6	54	20
Hip.....	8.6	37	20	11	2
Hand.....	13.6	5	45	9	41
Wrist.....	8.6	19	54	4	23
Elbow.....	6.0	44	29	0	27
Shoulder...	6.9	33	56	0	11
Sacroiliac..	8.6	25	21	50	4
Spine.....	10.3	25	2	53	20

The correlation between the particular joint involved and the type of pathology is most striking. It is so marked as to suggest that the type of reaction is due rather to the location of the disease than to its etiology. There is, for example, a complete absence of the hypertrophic group in the shoulder and elbow while in the knee and spine the percentage of joints of the atrophic type is very small. It is also notable that the hands show the highest percentage of involvement of the infectious type. This may also be related to the early occurrence of the disease in the joints of the hands.

TABLE III

AGE OF PATIENT RELATIVE TO TYPE OF INVOLVEMENT

Age	Percentage of Total	Percentage of Normal	Percentage of Atrophic	Percentage of Hypertrophic	Percentage of Infectious
20–29	4.3	40	48	12	0
30–39	16.2	46	43	4	7
40–49	22.2	44	28	25	3
50–59	41.8	13	28	28	31
60–69	7.4	9	26	36	29
70+	5.1	17	3	31	49

In Table III is shown the relationship of the age of the patient to the type of disease present. The joints in the age group from ten to nineteen years were so few that they were not considered. The first column gives the age distribution of the joints and it will be noted that 64 per cent occur between the ages of forty and fifty-nine. The succeeding columns show the distribution of the various types of involvement by age. A striking drop in the percentage of normal joints occurs after the fifth decade. This is possibly associated with the greater duration of the disease in these older individuals and their tendency to show hypertrophic changes which are more obvious on roentgen examination. The number of joints in the atrophic group drops rather sharply after the fourth decade while the number of those in the hypertrophic group increases very markedly at this same period. The prevalence of changes of the infectious type is very much greater in the later decades than in the earlier ones, tending to support the opinion that this group is simply a longer standing, more extreme phase of atrophic arthritis. These findings appear to establish clearly a definite correlation between the age of the individual and the type of pathology which affects his joints.

TABLE IV

DURATION OF ILLNESS RELATIVE TO TYPE OF INVOLVEMENT

Duration	Percentage of Normal	Percentage of Atrophic	Percentage of Hypertrophic	Percentage of Infectious
Under 3 months	34	40	23	3
Under 5 years	34	35	21	14
Over 5 years	21	35	19	25

The tabulation of the duration of the disease in each joint, as given in Table IV, did not show any such significant correlations as cited above. The percentage of normal joints was much less in those which had been affected more than five years than in those affected less than five years. Nevertheless the fact that 21 per cent of the joints which had been afflicted more than five years appeared normal in the roentgenogram would indicate that even late in the disease a negative roentgenogram is of little significance. The definite increase in the number of joints of the infectious type with the greater duration of the disease is of some importance. It tends further to indicate that this combined destructive and hypertrophic reaction is simply an end-result of the proliferative form of arthritis.

TABLE V

DISTRIBUTION OF CASES AS TO TYPE OF INVOLVEMENT OF JOINTS

Type	Number of Cases	Percentage of Total
Normal joints only	4	7
Atrophic arthritis only	8	13
Hypertrophic arthritis only	8	13
Infectious arthritis only	5	8
Atrophic and hypertrophic arthritis	14	23
Atrophic and infectious arthritis	5	8
Hypertrophic and infectious arthritis	10	17
All three types	6	10
Total number of cases	60	100

In Table V is indicated the distribution of the 60 patients as to the types of arthritis which affected their joints. There were 4 cases in which none of the joints showed any changes. Of the remainder it may be noted that the three types occurring alone are fairly evenly divided, while the combination of atrophic and hypertrophic types in the same individual is by far the most frequent. The other combinations are also given. It is notable that 10 per cent of all the cases showed all three types of involvement in their joints (Fig. 4).

TABLE VI

MULTIPLICITY OF TYPES OF INVOLVEMENT

	Number of Cases	Per Cent
Pathological joints	56	
One type of involvement	21	37
Two types of involvement	29	52
Three types of involvement	6	11

A summary of the cases as to multiplicity of types of involvement is shown in Table VI. This indicates that almost two-thirds of the patients showed more than one variety of roentgen manifestations in their various joints. This high incidence of mixed types would seem to be significant as suggesting that the roentgen classification has little relation to the etiology or the clinical course of the disease.

A consideration of the findings tabulated above makes it apparent that negative roentgen findings have relatively little significance. The roentgen examination of the joints, nevertheless, is a most valuable procedure as it gives a fairly accurate picture of the gross pathological changes which are present. Once the cartilage and bone are affected by the disease, the roentgenogram will give invaluable information as to the nature and extent of the disease changes. The determination of the prognosis and method of treatment to be used may depend largely upon the roentgen findings. On the other hand, it seems evident that the roentgen findings in chronic arthritis have little direct relation to the etiology of the disease. These findings are influenced more by the localization in any particular joint, by the age of the patient, and by the duration of the illness than by any clinical entity or causative factor. This is particularly true of the so-called infectious group.

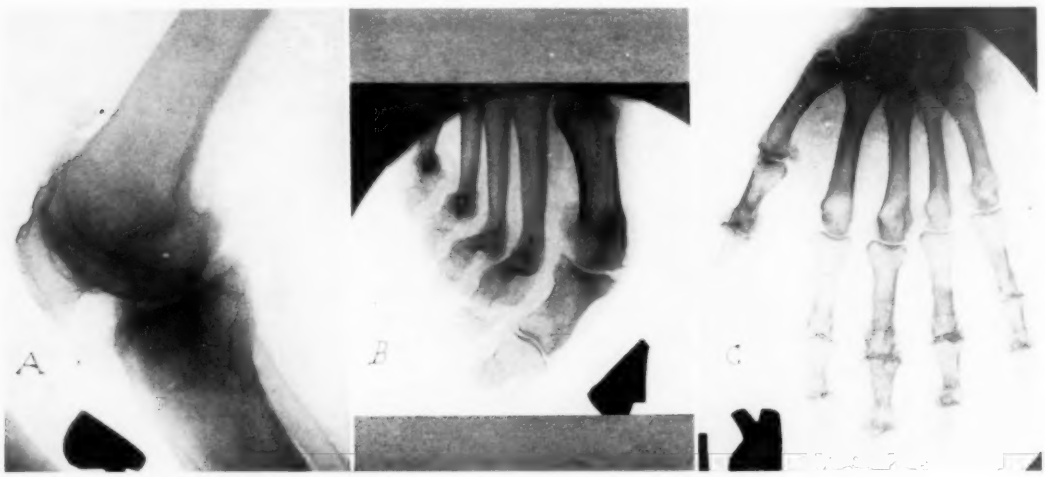

FIG. 4. Chronic arthritis with multiple types. Roentgenograms of knee (*A*), foot (*B*), and hand (*C*) from same case. Knee (*A*) shows typical picture of hypertrophic type of marked degree. Foot (*B*) shows typical appearance of atrophic type of marked degree. Note punched out areas near articular surface of first metatarsal resembling gout. Hand (*C*) shows fairly typical picture of "infectious" type with marked destruction and marked bone production, well shown in interphalangeal articulations. Clinically the findings in these three groups of joints were much the same.

In view of the absence of any more specific classification it seems reasonable to continue to use the terms atrophic and hypertrophic, corresponding to proliferative and degenerative indicating broad subdivisions of chronic arthritis. The group of cases designated above as "infectious" may better be considered either as of the atrophic group or a mixed type depending somewhat on the findings in the individual

case. That mixed types occur has been demonstrated in the studies of the pathology of arthritis,[4,8] and it is highly probable that many of these cases should be so classified. In addition it seems desirable to preserve a certain degree of sub-classification along anatomico-pathologic lines. For example, in the atrophic group, cases might be described as simple atrophic arthritis, atrophic arthritis with ulceration, atrophic arthritis with new bone formation. Likewise in the hypertrophic group, modifications of this broad term which are somewhat descriptive of the gross pathological changes observed should be attempted. In the light of our present knowledge, a descriptive classification, as advocated by Shapiro, appears to be the most satisfactory for roentgenologic purposes.

SUMMARY

Sixty cases of chronic polyarticular arthritis were studied by roentgen examination of all the affected joints, numbering 564.

On the basis of the roentgen findings the joints were classified into four groups: normal, atrophic, hypertrophic, and "infectious."

Over 25 per cent of the joints in this series appeared normal.

A significant correlation was found between the localization of the disease in certain joints and the type of reaction.

A significant correlation was found between the age of the patient and the type of involvement.

There was some correlation between the duration of the disease in the joint and the type of involvement, but it was not marked.

The division designated as "infectious" showed a close relation to the age of the patient and the duration of the illness. The older the patient and the longer the duration of the disease in any particular joint, the more frequently was this type found.

The cases studied presented a high percentage of mixed types of involvement of the joints. Almost two-thirds of the patients showed two or three types of reaction in various joints. Only 37 per cent of the patients showed a uniform type of pathology in all their joints.

CONCLUSIONS

While a negative roentgenogram is of little significance in chronic arthritis, positive findings are extremely valuable as indicating the extent and nature of the disease process. For roentgen purposes chronic arthritis should be divided into atrophic, hypertrophic, and mixed groups. It is desirable to use a descriptive classification with sub-groups to indicate the anatomico-pathologic changes which are present. The group designated as "infectious" arthritis should be abandoned.*

* For discussion see page 795.

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ROENTGENOLOGICAL STUDIES OF THE INTERVERTEBRAL DISC*

A DISCUSSION OF THE EMBRYOLOGY, ANATOMY, PHYSIOLOGY, CLINICAL AND EXPERIMENTAL PATHOLOGY

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THE intervertebral disc is of fundamental importance in the normal and pathological physiology of the spine. The nucleus pulposus or pulpy center of the intervertebral disc is not a vestigial remnant as earlier anatomists were led to believe, but is a living and essential part of the vertebrate spine.

Vesalius,[39] in 1555, described the intervertebral disc as a tough, fibrocartilaginous ligament with a soft center. Von Luschka[14] accurately described its structure and embryological development, while Bardeen,[3,4,5] in his studies of the development of the spine, postulated as to the physiological importance of the nucleus pulposus. Clinical and pathological studies of primary intervertebral disc lesions were not made until Schmorl,[27] a pathologist of Dresden, in 1926, described the frequent prolapses of the disc into the adjacent vertebral bodies.

The roentgenological recognition of the prolapses of the intervertebral disc into the vertebral bodies was first demonstrated by Mau[15] in 1928 and Dittrich[9] in 1929. Each author reported single cases of pain in the back and disability, where the lateral roentgenograms showed the punched out areas in the vertebral bodies just adjacent to the portion of the intervertebral disc which is normally occupied by the nucleus pulposus. Subsequent studies by Müller,[19] Sashin,[25] Geist,[10] Beadle,[6] and Calvé and Galland[7,8] have also demonstrated prolapses of the nucleus pulposus into the adjacent vertebral bodies by means of the roentgen ray.

THE ANATOMY OF THE INTERVERTEBRAL DISC

The roentgenological evaluation of lesions of the intervertebral disc requires some knowledge of the developmental and structural anatomy of the disc and its components.

The nucleus pulposus of the intervertebral disc develops from the notochord. Kollmann,[13] Bardeen,[3,4,5] and Minot[16,17] are agreed that the notochord is derived from the entoderm. A migration of mesenchymal cells occurs from the sclerotomes and surrounds the notochord. Remak[22] and Bardeen believe these cells arrange themselves in a segmented column in accordance with the primitive segmentation of the embryo. From our studies we are led to agree with Williams,[41] as opposed to Bardeen's theory, that the early demarcation of the vertebrae is the result of differential growth and not one of cell condensation. The mesenchymal cells, arranged about the notochord, are at first almost entirely nuclei. When they begin to add cytoplasm those cells nearest the intersegmental artery, which enters the column of cells at points approximating the center of the future vertebral body, are better nourished and add cytoplasm more rapidly than do those farther away in the intervertebral region. The cells in this latter area acquire little cytoplasm and remain undifferentiated, forming the anlage of the intervertebral disc. It is of interest that this portion of the spine remains avascular throughout developmental and adult life (Fig. 1).

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As the cells of the vertebral regions increase in size from the added cytoplasm they begin to encroach upon the notochord and the cells of this structure are gradually extruded into the intervertebral regions where the pressure is less (Fig. 2).

In the ten weeks' embryo the cells of the vertebral bodies have developed into typical cartilage cells and ossification centers are present. The cells of the notochord have all been extruded from the vertebral region and are now confined to the central portion of the intervertebral disc, while the old site of the notochord in the vertebral bodies is marked only by a streak of mucoid material. The cells of the intervertebral region resemble fibrocartilage and are arranged along a vertical axis, attaching above and below to the vertebral bodies. From this age on, the notochord mass may be termed the nucleus pulposus and the surrounding fibrocartilage is the annulus fibrosus (Fig. 3).

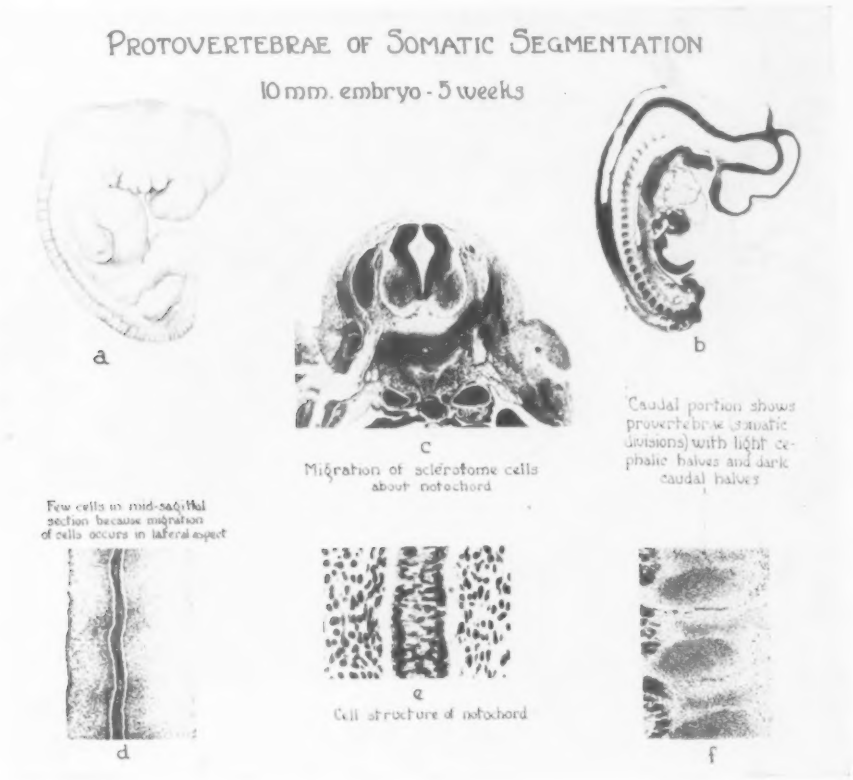

PROTOVERTEBRAE OF SOMATIC SEGMENTATION
10 mm. embryo - 5 weeks
a
b
Caudal portion shows protovertebrae (somatic divisions) with light cephalic halves and dark caudal halves
c
Migration of sclerotome cells about notochord
Few cells in mid-sagittal section because migration of cells occurs in lateral aspect
d
e
Cell structure of notochord
f

Fig. 1. A 10 mm. (5 week) human embryo. *a*. Lateral drawing of specimen showing somatic segmentation. *b*. Mid-sagittal section of specimen. Notochord with segmental flexures of Minot. Detailed structure of notochord in sections *d* and *e*. The primitive segmentation (protovertebrae) of Bardeen is well demonstrated in the caudal portion of this specimen with advancement toward the definitive stage cephalically. These segments are marked off above and below by the intersegmental arteries (see section *f*). Note the light cephalic half and dark caudal half of each protovertebra and the beginning differentiation and addition of cytoplasm of these two areas in the region of the intersegmental artery. *c*. Mid-dorsal cross section. Note the migration of the mesenchymal cells from the sclerotome to surround the notochord. These cells are massed laterally leaving the true mid-sagittal plane relatively less dense. (Series H 904 b, Slide 6, University of Chicago, Hull Anatomical Laboratory.)

Progressive mucoid degeneration of the notochord cells may be noted from this time and in the full term fetus and fourteen month old child fine strands of fibrocartilage are becoming more numerous in

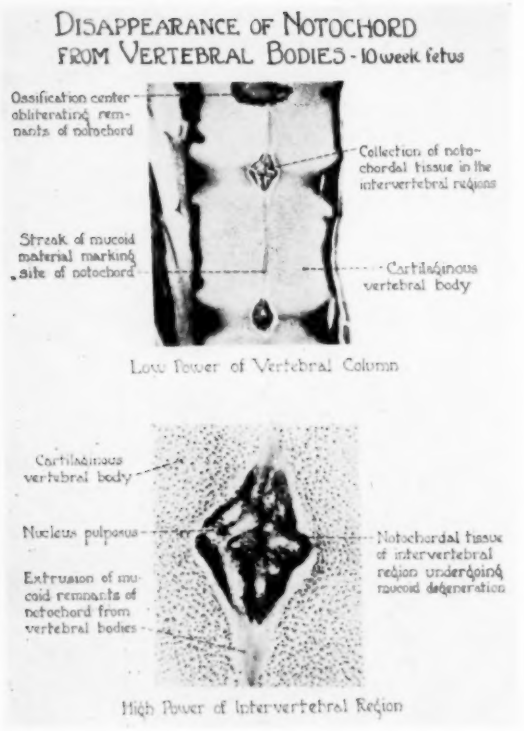

DISAPPEARANCE OF NOTOCHORD FROM VERTEBRAL BODIES - 10 week fetus
Ossification center obliterating remnants of notochord
Collection of notochordal tissue in the intervertebral regions
Streak of mucoid material marking site of notochord
Cartilaginous vertebral body
Low Power of Vertebral Column
Cartilaginous vertebral body
Nucleus pulposus
Extrusion of mucoid remnants of notochord from vertebral bodies
Notochordal tissue of intervertebral region undergoing mucoid degeneration
High Power of Intervertebral Region

FIG. 2. A 57 mm. (10 week) human embryo. The notochord cells are entirely extruded from the vertebral into the intervertebral region. Only a mucoid streak marks the old site of the notochord in the vertebrae. Ossification centers are now forming in the vertebral bodies and these destroy all traces of the notochord.

the nucleus pulposus. At term the intervertebral disc consists of this nucleus pulposus which is confined by a thick cartilage plate above and below, separating it from the vertebral bodies, and the annulus fibrosus, a circumferential lamellar layer the tough fibers of which are firmly attached to the edges of the adjacent vertebrae.

In the human there are normally 23 intervertebral discs, or one for each presacral intervertebral region. This adult intervertebral disc is made up of three components: the annulus fibrosus, the nucleus pulposus and two thin cartilage plates which overlie very thin layers of cortical bone of the vertebrae and confine the nucleus pulposus above and below (Fig. 4).

In dises unaffected by pathological processes, the nucleus pulposus retains its semigelatinous consistency even beyond the fifth or sixth decade, and upon sectioning the fresh specimen it is partially extruded by the elasticity of the annulus fibrosus.

FUNCTION OF THE INTERVERTEBRAL DISC

The nucleus pulposus is a fibrogelatinous material subject to the laws of fluids. It may be considered, therefore, incompressible and confined to its normal shape and position by the strong and elastic annulus fibrosus (Fig. 5). The elastic tension of the latter, which extrudes the nucleus pulposus material in the living organism, is not only the result of the elastic tension of the annulus fibrosus but also that of

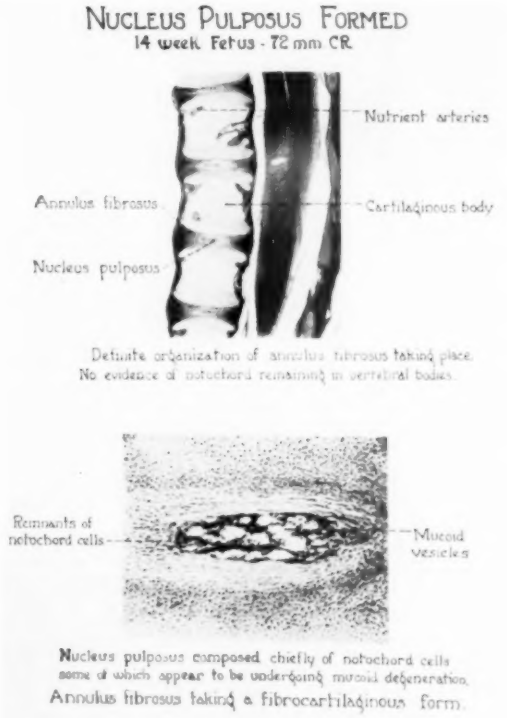
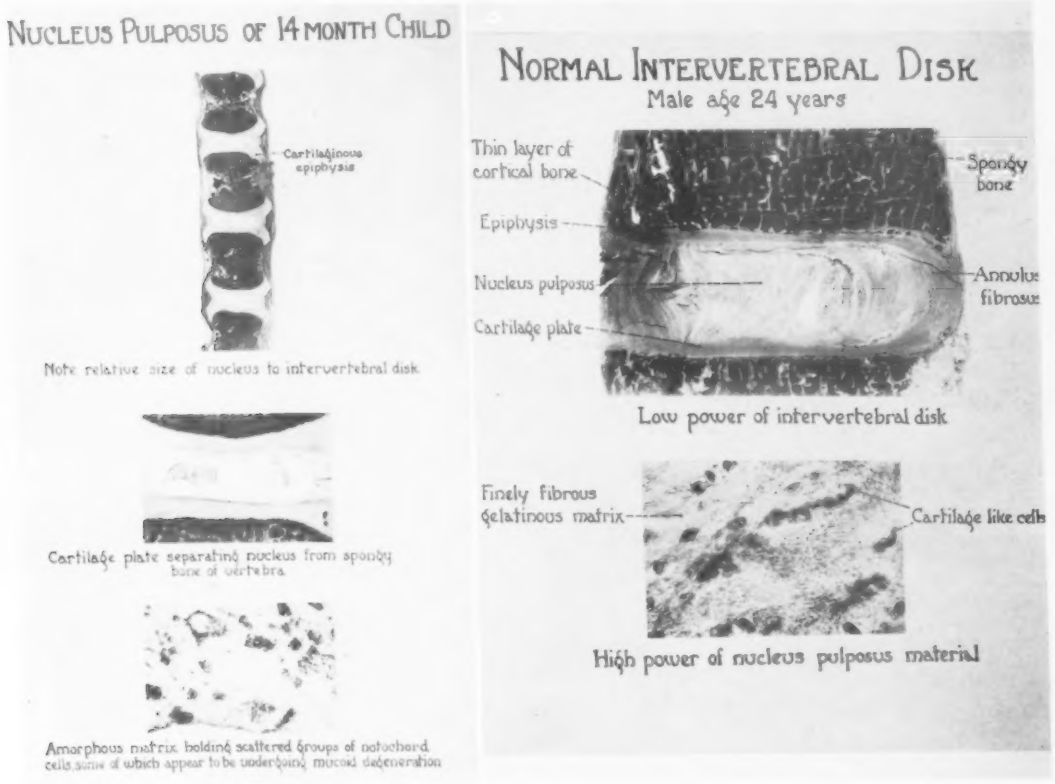

NUCLEUS PULPOSUS FORMED
14 week Fetus - 72 mm CR
Nutrient arteries
Annulus fibrosus
Cartilaginous body
Nucleus pulposus
Definite organization of annulus fibrosus taking place. No evidence of notochord remaining in vertebral bodies.
Remnants of notochord cells
Mucoid vesicles
Nucleus pulposus composed chiefly of notochord cells some of which appear to be undergoing mucoid degeneration. Annulus fibrosus taking a fibrocartilaginous form.

FIG. 3. A 72 mm. (14 week) human embryo. Midsagittal section of specimen. In the high power photomicrograph, the intervertebral disc shows a definitely fibrous annulus fibrosus surrounding a large mucoid nucleus pulposus. They form thereby a fibrous or fibrocartilaginous envelope about the nucleus pulposus.

muscle tone and static forces transmitted from one vertebral body to the next. The proper function of the nucleus pulposus therefore depends upon the integrity of its limiting structures, viz., the cartilage plate above and below and the surrounding annulus fibrosus. The primary hypothesis of incompressibility of the nucleus pulposus demands that any compression of the intervertebral disc must result from the change of shape of the nucleus pulposus at the expense of the elastic annulus fibrosus. The amount of compression of the intervertebral disc will therefore depend upon the elasticity and strength of this structure. From observation of this fibrocartilaginous ring we may postulate that only minor changes may take place under the forces to which it is exposed. These changes, however, are sufficient to give the intervertebral disc enough resiliency to absorb the shocks transmitted along the vertebral column. The incompressibility of this portion of the intervertebral disc lends to it the function of transmitting the static and muscular forces from one vertebral body to the next and establishes it as the axis of motion upon which each vertebral body must work.


Nucleus Pulposus of 14 month Child
Cartilaginous epiphysis
Note relative size of nucleus to intervertebral disk
Cartilage plate separating nucleus from spongy bone of vertebra
Amorphous matrix holding scattered groups of notochord cells some of which appear to be undergoing mucoid degeneration
Normal Intervertebral Disk
Male age 24 years
Thin layer of cortical bone
Spongy bone
Epiphysis
Nucleus pulposus
Annulus fibrosus
Cartilage plate
Low power of intervertebral disk
Finely fibrous gelatinous matrix
Cartilage like cells
High power of nucleus pulposus material

A B

Fig. 4. *A*. Normal sagittal section of the spine of a fourteen month old child. *B*. Normal intervertebral disc of a twenty-four year old male (1st lumbar).

Pathology of the Intervertebral Disc

The pathological physiology of the intervertebral disc can be best understood if one keeps constantly in mind the fact that the nucleus pulposus is the medium of transmitting pressure from one vertebra to the next. On the surface of each disc a pressure force is exerted on the concave side and a depression force on the convex side. These forces counterbalance each other, but the

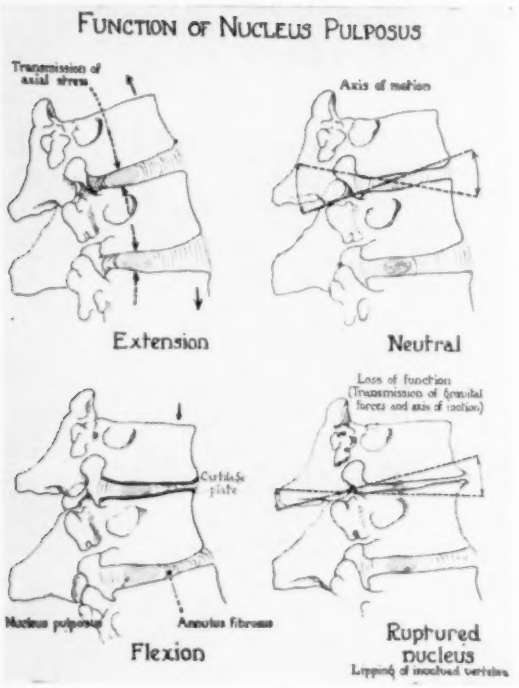


FIG. 5. A diagrammatic sketch illustrating the function of the intervertebral disc.

force of gravity persists on the nucleus which transmits the weight from one vertebra to the next by the intermediary of the nuclear axis. Any pathological process which weakens the structures confining the nucleus pulposus, invades the nucleus itself, or merely allows portions of the nuclear material to escape, will interfere with the normal function of the spine.

Symptoms, characterized by pain in the back and disability, may not be expected in the spine with minute ruptures of the cartilage plate and small extrusions of the nuclear material. Schmorl concluded from his studies that the nuclear prolapses which he found in 38 per cent of the spines which he studied at autopsy were of little clinical significance, but he reviewed the histories of only 5 of the patients which were autopsied in his institute. Beadle[6] suggested the course of the pathological processes in a number of clinical conditions affecting the spine, but the part played by the nucleus pulposus lesions them-

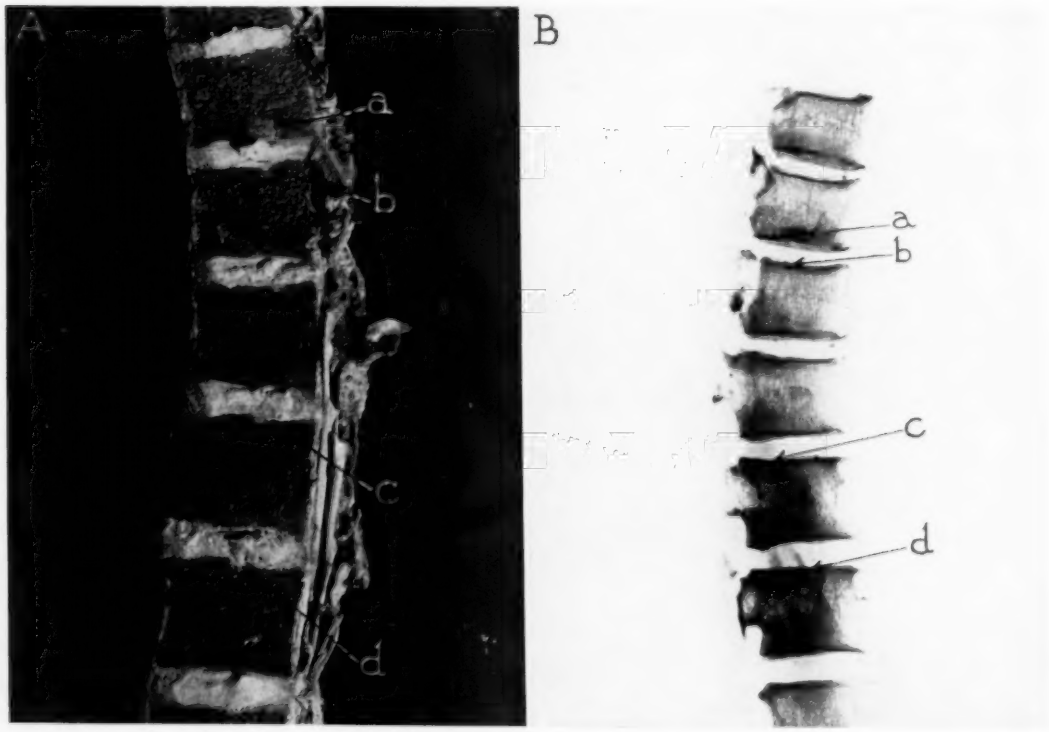


FIG. 6. Several ruptures of the nuclei pulposi (*a*, *b*, *c*, *d*) are noted in the gross specimen, *A*, but only the large prolapse (*a*) can be clearly recognized in the roentgenogram *B*.

selves has not been satisfactorily defined.

Jung and Brunschwig[11] have recently studied the innervation of the articulations of the vertebral bodies and have demonstrated sensory nerves in the anterior longitudinal ligament, but no nerve fibers of any kind were found in the intervertebral disc. For this reason trauma or disease affecting the intervertebral disc can produce subjective symptoms only in proportion to the degree to which the adjacent structures are involved.

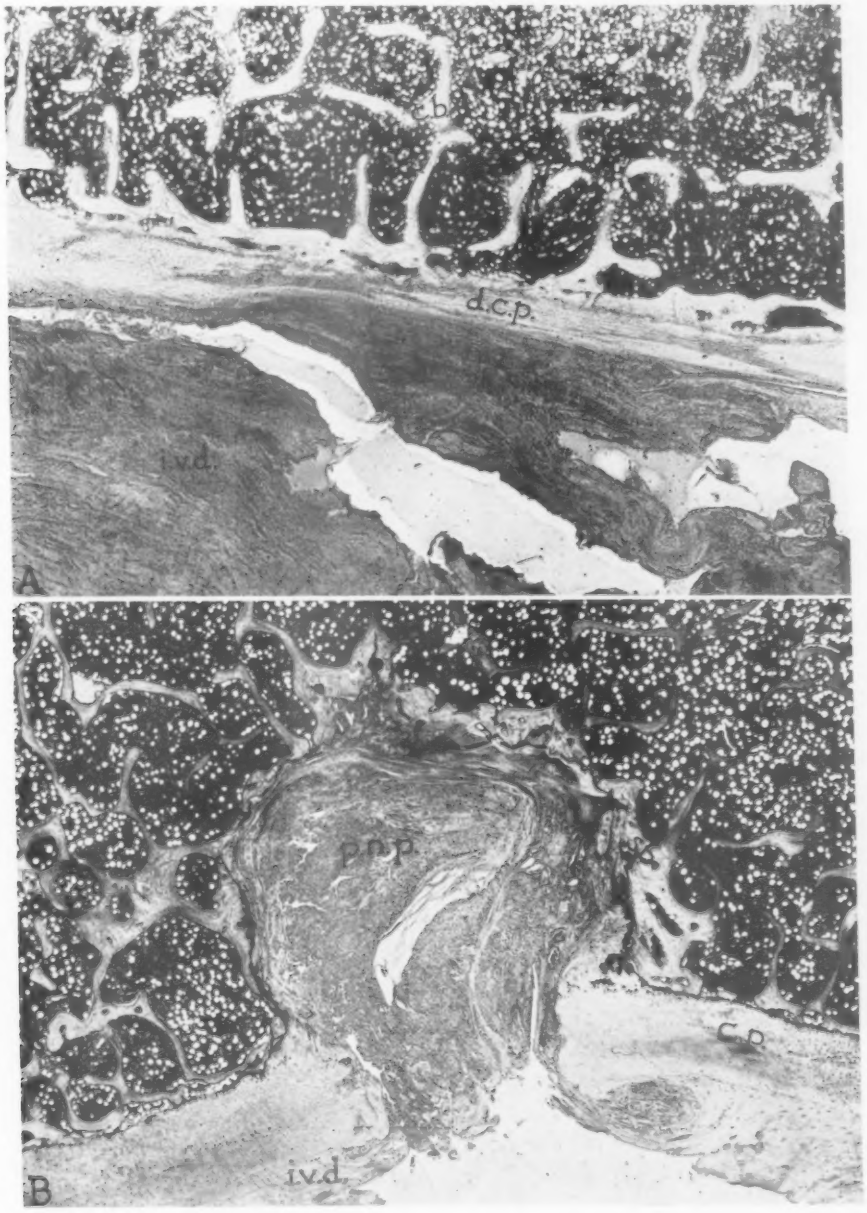


Fig. 6*a*. Fibrillation of the cartilage plate (*d.c.p.*) is demonstrated in *A*. In *B* the plate has ruptured and nucleus pulposus material of the intervertebral disc (*i.v.d.*) is streaming through. A cartilage nodule (*p.n.p.*) has been formed and a zone of sclerosed bone (*s.b.*) is noted about it.

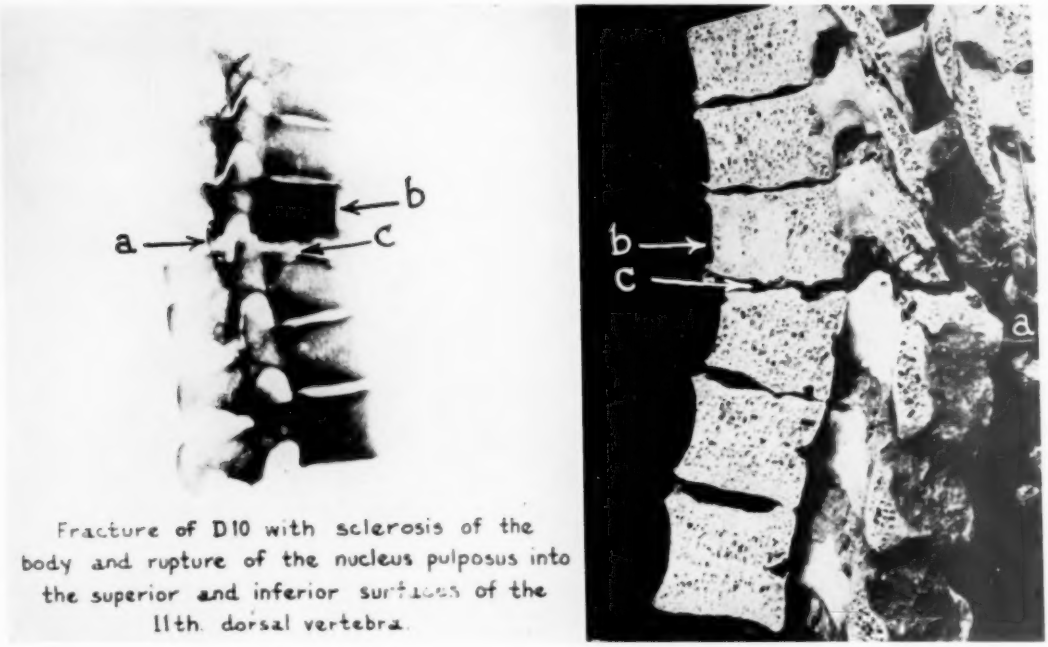

a
b
c
Fracture of D10 with sclerosis of the body and rupture of the nucleus pulposus into the superior and inferior surfaces of the 11th dorsal vertebra.
b
c
a

FIG. 7. This specimen was taken from a patient who died of an intercurrent infection several years after he was treated by Dr. Phemister for a compression fracture of the 10th thoracic vertebra. The dense sclerosis of the 10th dorsal vertebra is noted in both the roentgenogram and the sagittal section of the gross specimen. The large ruptures in the articular surfaces of D 11 may be explained on the basis of the injury. The sclerosis and osteophyte formation may have resulted from the erosion and loss of the intervertebral discs which followed extrusion of the nucleus pulposus material into the vertebrae.

ROENTGENOLOGIC DIAGNOSIS OF NUCLEAR PROLAPSES

The commonest lesion of the spine, according to Schmorl, and confirmed by our observations, is the prolapse of the nucleus pulposus into the spongiosa of the vertebral body. The mere presence of these cartilaginous nodules may not cause pain in the back. The nuclear material is extruded through a crack or other defect in the cartilage plate into the spongy bone by the force which is transmitted to that disc by the weight of the body and by the tone of the spinal muscles and ligaments. As a result of this invasion a reaction is set up in the bone. The semi-fluid material is transformed into a cartilage nodule and the bone about it becomes sclerosed, forming a secondary line of defense to wall off the invading material (Fig. 6). This sclerosed bone about the nodule may be noted in the roentgenogram, but until sufficient time has elapsed following the prolapse of the nuclear material of the disc for the reaction in the bone to take place, the roentgen diagnosis usually cannot be made.

If only a small portion of the nucleus pulposus is extruded, the function of the intervertebral disc may not be seriously affected, and no immediate disability would be expected. The extrusion, however, of even minute portions of the semi-gelatinous nucleus pulposus may open avenues for dehydration of the disc and hence diminished function at an earlier age than such changes normally occur. This has been shown by the studies of Püschel[21] and has been confirmed by us. We believe that such small ruptures may thus be a predisposing etiological factor in the development of arthritis of the spine years later.

If a considerable portion of the semi-fluid material escapes either into the

spongy bone or through the fibers of the annulus fibrosus, the weight of the body and the trauma of every-day life can no longer be transmitted from one vertebral body to the next through this semi-fluid cushion, but must be borne in part by the fibrocartilaginous annulus fibrosus. The intervertebral disc then becomes thinner and in some instances completely wears out. When the nucleus pulposus has been destroyed, the axis of motion is shifted posteriorly to the articular facets and the weight of the body, especially in all forward or lateral bending, is transferred to the lateral or anterior portion of the vertebral bodies themselves (Fig. 7). As a result of this the adjacent vertebrae may become sclerosed and the lipping and spurs characteristic of osteoarthritis of the spine will be noted in the roentgen examination. If the vertebral body has been softened by disease such as tuberculosis or neoplasm, it may be eroded and ultimately completely destroyed (Fig. 8).

CLINICAL STUDIES OF THE INTERVERTEBRAL DISC

Fifty-nine years before Schmorl engaged the interest of pathologists in the nucleus prolapses noted upon section of the spine at autopsy, Virchow,[40] in 1857, described a tumor found upon the inner surface of the base of the skull, and believing it to be a growth of cartilage, named it ecchondrosis physalifora. Müller,[18] one year later, tried to show that this tumor was derived from notochordal tissue, and Steiner[38] in 1894, after a careful study of a similar case, concluded that Müller was correct in this hypothesis. Their work did not lead to further studies of the nucleus pulposus.

Calvé and Galland[7] in 1922, and Bársony

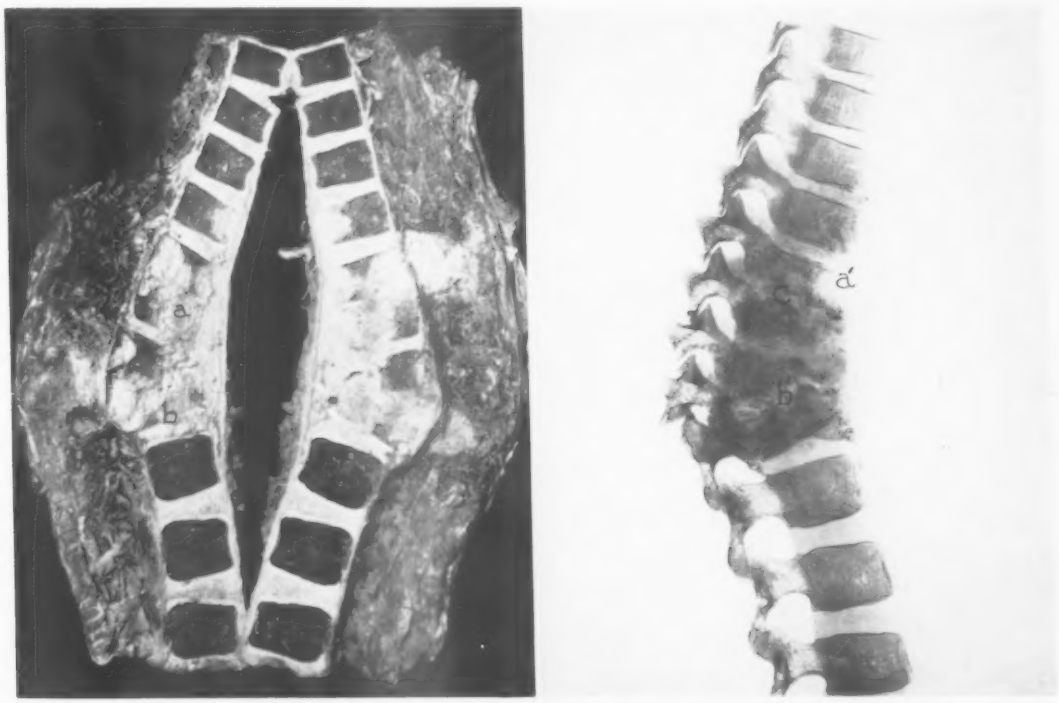


Fig. 8. The pathology of tuberculosis of the spine is demonstrated in this gross specimen. Several vertebral bodies have been destroyed and the spinal cord has been compressed at the apex of the kyphosis. Tuberculous material is extending upward along the vertebral bodies under the anterior longitudinal ligaments and invading additional vertebral bodies and discs (a'). The cancellous bone has been completely replaced by caseous tuberculosis (a), while at (b) the cartilage plate has been eroded and the disease is beginning to invade the disc. At c and b' the intervertebral discs have been completely destroyed.

and Polgár[2] in 1925 described calcification of the nucleus pulposus. Schmorl in 1926 and 1927 reported that 38 per cent of the spines which he routinely sectioned at autopsy showed prolapses of disc material into the spongiosa of adjacent vertebral bodies. He attributed little clinical significance to these findings, but Schanz,[26] one year later, suggested the possibility of a direct causal relationship between these prolapses or cartilage nodes and backache. Mau[15] and Müller[19] in 1928 and Dittrich[9] in 1929, found evidence of nuclear prolapses characterized by sclerosis about punched out areas in the vertebral bodies as seen in the lateral roentgenograms of

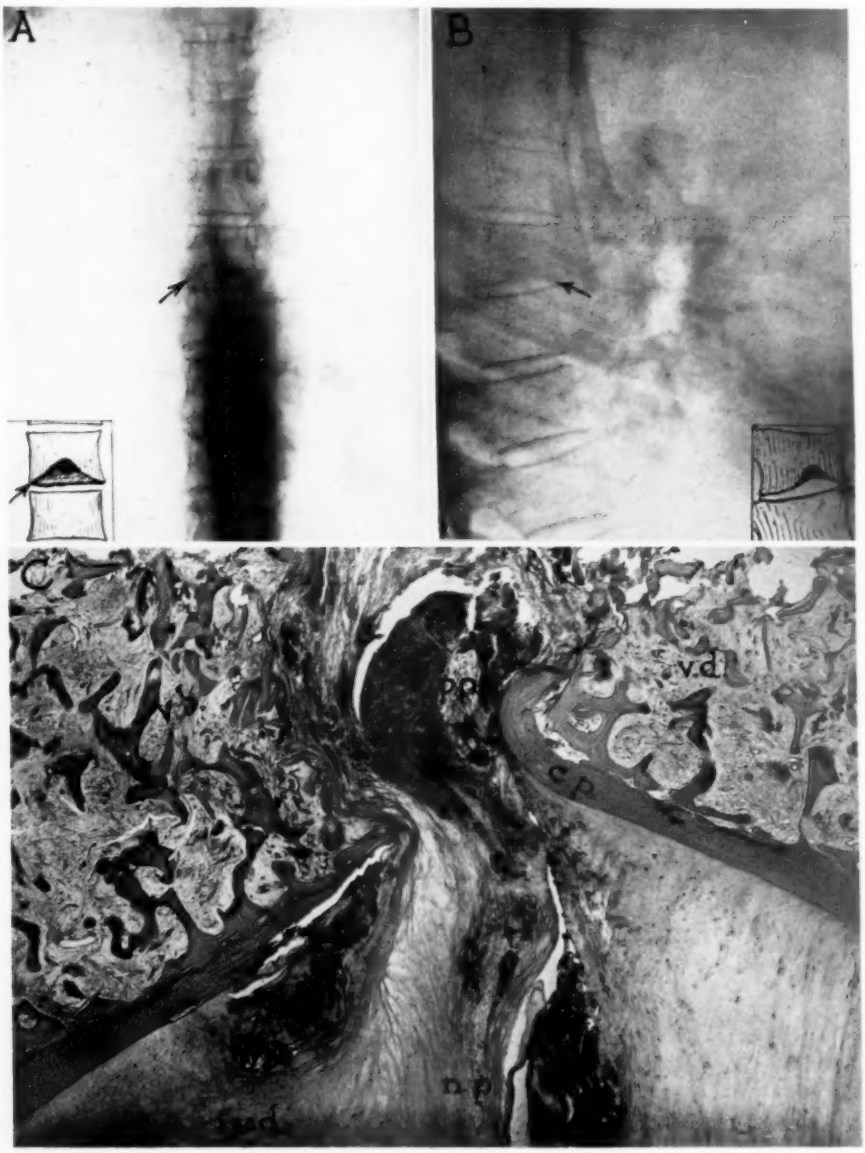


FIG. 9. Case 1. A single cone-shaped depression in the inferior surface of the 6th thoracic vertebra is indicated by the arrows. The intervertebral space is narrow and the anterior edges of the two vertebral bodies in *B* show beginning lipping. The artist's sketches emphasize and slightly exaggerate the roentgenological picture. *C* is a photomicrograph of a section of a similar rupture in a specimen removed at autopsy.

cases in which there was a history of pain in the back and disability.

Andrae[1] and Schmorl described prolapses of the nucleus pulposus posteriorly with extension of the disc into the spinal canal, and Calvé and Galland reported two clinical cases in which a diagnosis of this morbid anatomy in relation to certain spinal deformities.

Geist, Calvé and Galland, Sashin, and Beadle have enumerated a number of pathological conditions in which the intervertebral nucleus pulposus is either primarily or secondarily involved. In another

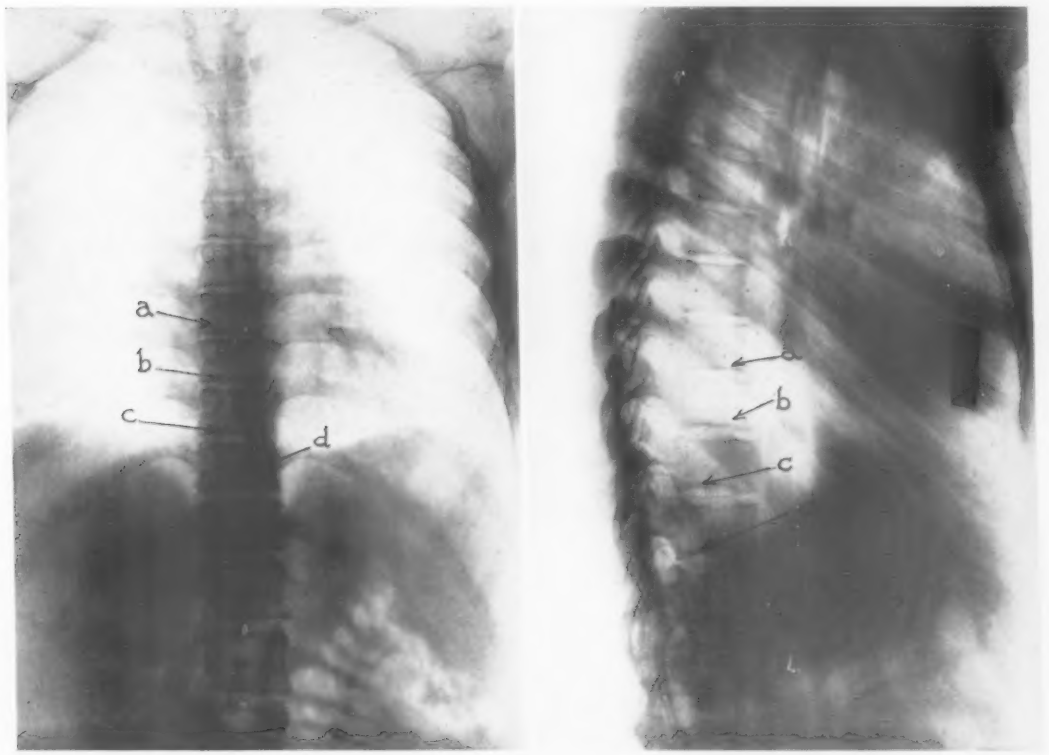


FIG. 10. Case II. In both the lateral and anteroposterior roentgenograms the intervertebral discs appear to be slightly narrowed and there are several punched out areas in the articular surfaces typical of prolapse of the nuclei pulposi (*a*, *b*, *c*).

condition was made. Many additional articles reporting single cases of lesions of the intervertebral disc, or autopsy findings, have appeared in the journals of the last three years, mostly in the German literature, while Geist[10] and Sashin,[25] as well as Calvé and Galland, have reviewed the work of Schmorl in American journals and have postulated regarding the clinical significance of the changes in the intervertebral nucleus pulposus.

In a very complete recapitulation of the entire subject of the intervertebral discs, Beadle[6] has discussed their normal and paper[12] we have attempted to classify the various lesions according to the primary location of the pathological process.

No attempt will be made to repeat that classification at this time. Any disease process which may weaken the static structure of the vertebral body, such as osteomalacia, malignancy, or tuberculosis, may result in central compression of the vertebral body, rupture of the cartilage plate and extrusion of the nucleus pulposus into the spongy bone. Breaks in the cartilage plate from chronic or acute trauma, disease, or congenital defect due to incomplete

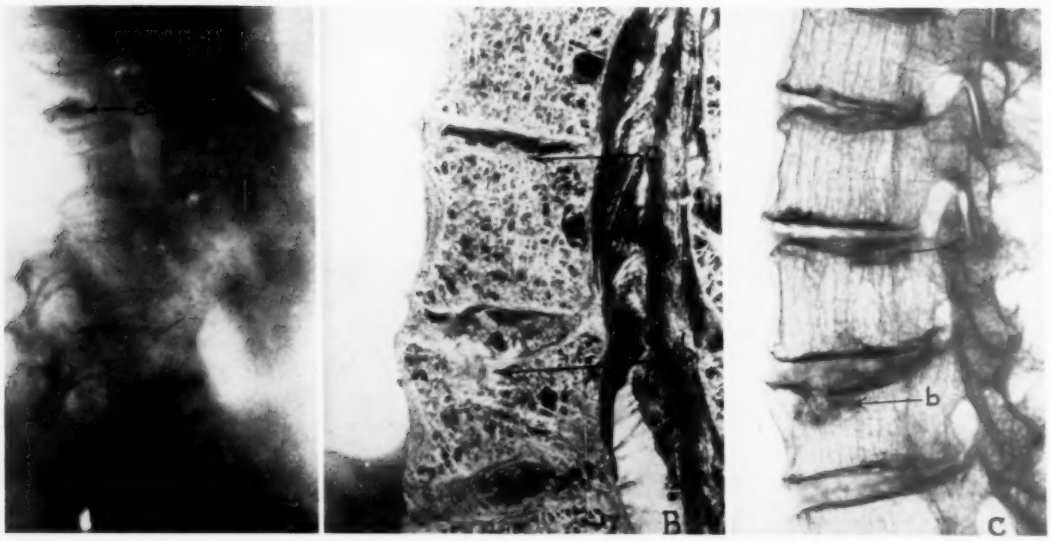


FIG. 11. Case III. *A*. Lateral roentgenogram of spine of a patient with Paget's disease and metastatic osteogenic sarcoma. There are several biconcave vertebral bodies and one large rupture of the nucleus pulposus (*a*) with an unusual amount of sclerosis in that region. It is thought that this may contain a metastatic lesion. *B*. Museum specimen of a spine showing marked osteoporosis. Vertebral bodies are biconcave and there are several breaks in the articular surface with sclerosed Schmorl's nodules (*a* and *b*) which can also be seen in the roentgenogram *C*.

closure at the site of the notochord, may permit single or multiple prolapses of nuclear material into the adjacent vertebral body. The nucleus pulposus may become shifted forward or backward, thus changing the center of the axis of motion and disturbing the balance of the spine. Retropulsion backwards into the spinal canal has been described. In scoliosis this nucleus has been found shifted to the side of the convexity of the curvature and, while Schmorl was not able to find evidence that this was in any way an etiological factor in the production of scoliosis, this shift of the non-compressible nucleus may be the explanation of much of the difficulty found in attempts to correct the lateral curvature.

FIG. 12. Case IV. The calcified nucleus pulposus is clearly visualized in both the lateral and the anteroposterior views.

Lesions of the spine in which the intervertebral discs are either primarily or secondarily involved are relatively common in every large orthopedic clinic. Most of these lesions may be diagnosed by a careful roentgenographic examination in which a good lateral plate is most important. The following cases are presented to illustrate the clinical history and roentgenological findings characteristic of a few of the more common lesions of the intervertebral disc.

REPORT OF CASES

Case I. *Single Prolapse of the Nucleus Pulposus.* E.N., female, aged thirty-two. Patient complained of back pain of two years' duration. At onset she had noted rigidity of the spine, most marked upon arising in the morning, and pain characterized by a dull ache in the upper dorsal region. She obtained some relief from placing boards on the bed springs to "splint the mattress." Fatigue caused an exacerbation of the pain. For three months prior to admission to the University Clinics the pain in the mid-thoracic region had become more marked with radicular involvement causing radiation of the pain along the course of the 6th intercostal nerve.

Roentgen Findings. Anteroposterior films of the dorsal spine showed central depression and a break in the inferior surface of the 6th thoracic vertebra. A lateral roentgenogram of this portion of the spine showed anterior wedging of the 6th thoracic vertebra in addition to the cone-shaped rupture in the inferior surface.

Comment. This lesion was diagnosed as an isolated rupture of the inferior cartilage plate of the 6th thoracic vertebra with prolapse of the nucleus pulposus material into the spongy bone producing localized symptoms. A back brace was advised. (Fig. 9.)

Fig. 13. Case v. The extensive destruction of vertebral bodies by the tuberculous process is illustrated both in the roentgenogram and the photomicrograph. The cartilage plate has been broken through and the nucleus pulposus has prolapsed (*p.n.p.*) into the diseased vertebral bodies. The intervertebral disc between the two diseased vertebrae has been almost completely destroyed (*d.i.v.d.*).

Case II. *Multiple Prolapses of Nuclear Material.* A.G., female, aged twenty-four. Three years before admission to the University of Chicago Clinics this patient fell, striking her back on the cellar steps. She was confined to bed for several months and her back was strapped with adhesive by the attending physician. The pain, which was confined to the dorsal spine, was not entirely relieved and she has continued to have intermittent attacks. This interfered with her occupation as a stenographer since fatigue and positional strain caused an increase in the backache. A slight

dorsum rotundum was noted in the physical examination. There was tenderness upon palpation and definitely decreased mobility of the lower dorsal spine.

Roentgen Findings. There was irregularity of the adjacent surfaces of the lower dorsal vertebrae and definite punched-out and sclerosed areas typical of the reaction about cartilaginous nodules described by Schmorl (Fig. 10).

crease in the density of the vertebral bodies with central compression of the softened vertebrae and definite breaks in the depressed surfaces of some of the vertebrae. Further studies led to the diagnosis given above, but the findings in the spine alone indicated a definite softening of the vertebral bodies with central excavation due to the pressure transmitted through the nucleus pulposus from one vertebral body to another

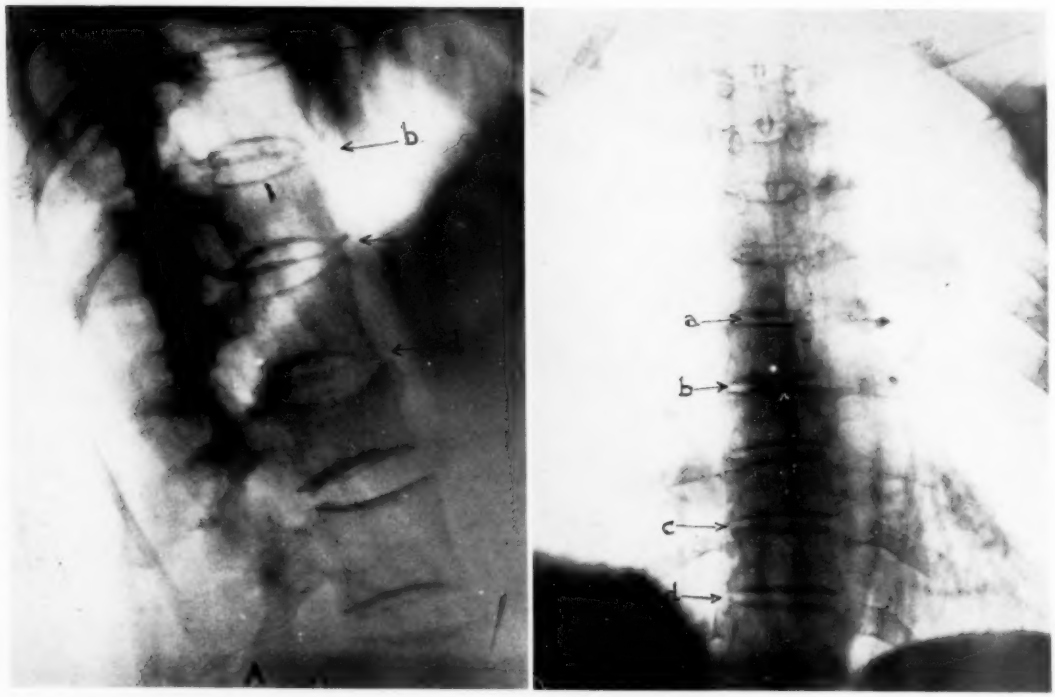


FIG. 14. CASE VI. *A.* Lateral view of this spine shows marked lipping of the anterior edges of adjacent vertebral bodies (*a*, *b*, *c*, *d*). There is also some tendency toward central compression of the vertebral bodies which is most marked in (*d*). *B.* In the anteroposterior view the articular portions of the vertebral bodies are roughened and lipping at edges of the bodies is also noted (*a*, *b*). Small areas of calcification in the lateral longitudinal ligaments are noted at (*c*) and (*d*) and the vertebral bodies of this side more nearly approximate each other due to narrowing of the intervertebral disc than on the opposite side of the spine.

Comment. A Taylor back brace was applied, affording moderate relief.

CASE III. *Osteitis Deformans (Paget's Disease) of the Pelvis with Osteogenic Sarcoma and Metastases to the Spine.* M.K., female, aged sixty-one. For two and one-half years before admission to the clinic this patient had complained of pain in the low back and in the left hip region. The pain was made worse by exercise and, in spite of treatment by means of physiotherapy and a sacroiliac belt, the disability had become much more marked.

Roentgen Findings. There was marked de-

and subsequent rupture of the cartilage plate and extrusion of the nucleus pulposus material (Fig. 11).

Comment. The condition described in this spine may be reproduced by any disease process which causes softening or destruction of a vertebral body. Such conditions include: osteomalacia, metastatic neoplasm, senile osteoporosis and tuberculosis.

CASE IV. *Calcification of the Nucleus Pulposus*, E.L., female, aged forty. (Bone and Joint Service of University of Michigan.) Complained of pain in the lower dorsal region of the

spine penetrating through to the abdomen, worse in the morning and during activity. Examination revealed a full range of motion in the spine without any muscle spasm.

Roentgen Findings. Roentgenograms revealed a calcified mass in the intervertebral disc between the tenth and eleventh dorsal vertebrae. This was confined to the portion of the disc just posterior to the middle third which is typically occupied by the nucleus pulposus.

Comment. She has been somewhat relieved by wearing a corset (Fig. 12).

Case v. *Tuberculosis of the Spine.* C.C., female, aged thirteen. This patient had complained of pain in the back for six years and she had been treated for tuberculosis of the lumbar spine by means of casts and rest in bed until coming to our clinic.

Roentgen Findings. Roentgenograms showed a destructive lesion of the second, third, and fourth lumbar vertebrae with loss of the intervening intervertebral discs.

Comment. The patient died of tuberculous meningitis one month after fusion of the spine and the diseased portion of the spine was removed at autopsy. This revealed destruction of the intervertebral discs with extension of the nucleus pulposus material into the vertebral bodies (Fig. 13).

Case vi. *Chronic Degenerative Arthritis of the Spine.* N.A., female, aged sixty-three. This patient complained of pain upon motion of any part of the spine, of two years' duration.

Examination revealed a moderate dorsum rotundum, prominence and tenderness of the spinous processes of the 1st and 8th thoracic vertebrae and limitation of motion of the spine in all directions.

Roentgen Findings. The films of the cervical spine showed moderate lipping of the bodies of the 6th and 7th cervical and 1st and 2nd thoracic vertebrae. There was a slight kyphosis and left lateral scoliosis in the lower dorsal and lumbar spine. All of the bodies showed moderate lipping and cupping and the intervertebral spaces were narrow. The first lumbar vertebra

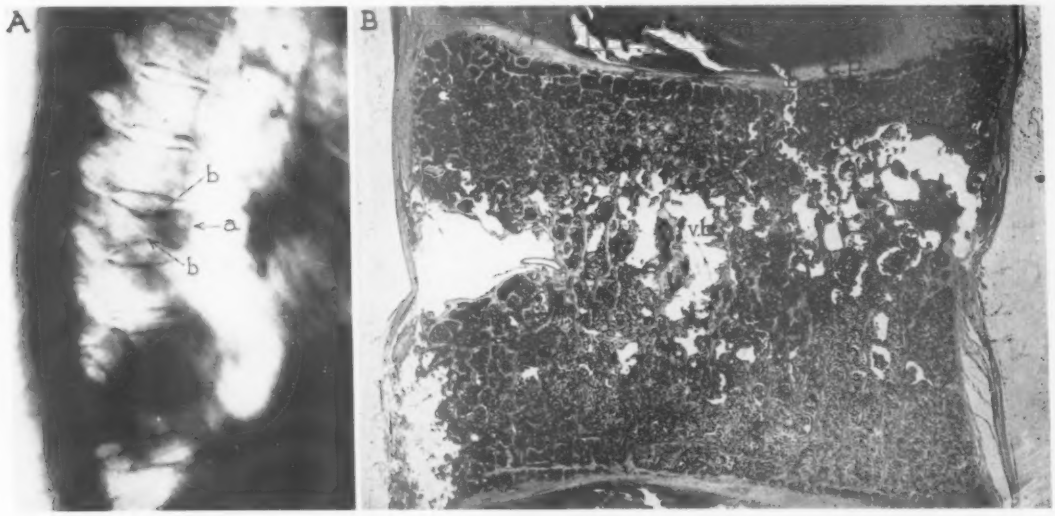


Fig. 15. Case vii. *A.* Shows a compression fracture of the 8th thoracic vertebra with flattening and increase in the anterior posterior diameter of the vertebral body. There is a depression in both the superior and inferior surfaces of this body (*b*) and the anterior half of the vertebral body shows an increased density (*a*) suggesting the possibility of the disturbance of circulation in this portion due to division of the vertebra by extrusion of nucleus pulposus material from both intervertebral discs and thus creating a cartilage mass which may have prevented normal healing of the fracture. Such a condition has been demonstrated in some of the specimens studied by Schmorl.

An acute compression fracture of the vertebral body is noted in *B*. This was taken from a patient who committed suicide by jumping from a fifth story window of the hospital. The extensive injury to the body of the vertebra (*f.v.b*) and the break (*b*) in the cartilage plate (*c.p.*) is illustrated. Had the patient lived and returned to normal activity, nucleus pulposus material (*n.p.*) would no doubt have been gradually extruded through this defect and into the vertebral body. We have produced such a condition experimentally in dogs.

was markedly decreased in size and moderately deformed. A generalized decalcification and atrophy of bone structures were noted. The lateral film merely emphasized the findings described above, and in addition showed small defects in the articulating surfaces of several vertebral bodies (Fig. 14).

FIG. 16. Case VIII. In this anteroposterior roentgenogram the intervertebral spaces are extremely narrow and numerous punched out areas in the articular surfaces of the vertebrae are indicated by the arrows.

Comment. Osteo- or degenerative arthritis is thought to be due in part to the wear and tear of the repeated trauma to which everyone is daily subjected. Schmorl concluded from his studies that minute prolapses of the nucleus pulposus material opened avenues through which further fluid loss might take place. This led to dehydration of the discs and resulted in progressive decrease in their normal function in the spine. As a result of the narrowing of the intervertebral discs, the wear and tear on the vertebral bodies is increased. The adjacent surfaces may become sclerosed, while the anterior edges of the vertebral bodies develop exostoses or spurs comparable to the hyperostoses which result from shoe pressure and irritation over a bunion. Our own experimental results lead us to agree with Schmorl that this may be the etiology of degenerative or osteoarthritis of the spine.

CASE VII. *Compression Fracture of Spine.* M.P., female, aged thirty-four. Patient came to the clinic complaining of severe pain in the lower dorsal spine. She dated the onset from a fall while descending the stairs in a store. As she fell she struck the left side of the spine against the stair rail and an elevator door. Further questioning elicited the history of a fall several years before, when she struck a radiator. She experienced severe pain in the lower dorsal spine and was disabled for nearly a year. Roentgenograms at that time were reported to be negative. Examination revealed marked tenderness, muscle spasm and limitation of motion in the lower dorsal spine.

Roentgen Findings. Roentgen observations of the spine at the time of her admission to the Orthopaedic Clinic revealed a compression fracture of the 8th thoracic vertebra (Fig. 15).

Comment. Schmorl has found at autopsy cases of compression fractures of vertebral bodies which did not unite because of extension of nucleus pulposus material into the defect and formation of a non-ossifying cartilage body. It is possible that the injury sustained by this patient several years before may have cracked the cartilage plate and permitted extrusion of nucleus pulposus material into the spongy bone, predisposing the vertebra to collapse. This type of an injury may be the explanation of Kümmell's disease.

CASE VIII. *Juvenile Kyphosis.* J.W., female, aged twenty-six. Seven years ago this patient complained of "sore spots" over the spine for

which she was treated by a physician with very little relief. Two years later she was run over by an automobile, one wheel going over the dorsal spine. This injury confined her to bed for three weeks, after which she was allowed up without any type of support for her back. Since this accident the patient has noted a progressive round back deformity, with a "bearing down" feeling in the region of the dorsal spine. She was unable to lift heavy objects and at times complained of radiating pains along the course of the intercostal nerves. For six months before her first visit to the University of Chicago Clinics in July, 1930, the disability had become much more severe.

Physical examination at the time of this first visit revealed a marked dorsum rotundum of the spine. The spinous processes of D 11 and D 12 were prominent and there was tenderness over the lower dorsal spine on deep palpation and percussion. Muscle spasm was quite marked in this region. There was no evidence of any central nervous system involvement. The Wassermann and Kahn tests were negative.

A Taylor back brace was applied and worn for two years. For a few months the patient was helped by the brace, but the deformity of the spine became progressively more marked. With the increasing deformity the symptoms recurred in spite of the brace and the intercostal nerve pain became so severe that she was confined to her bed most of the time and could not rest without a sedative.

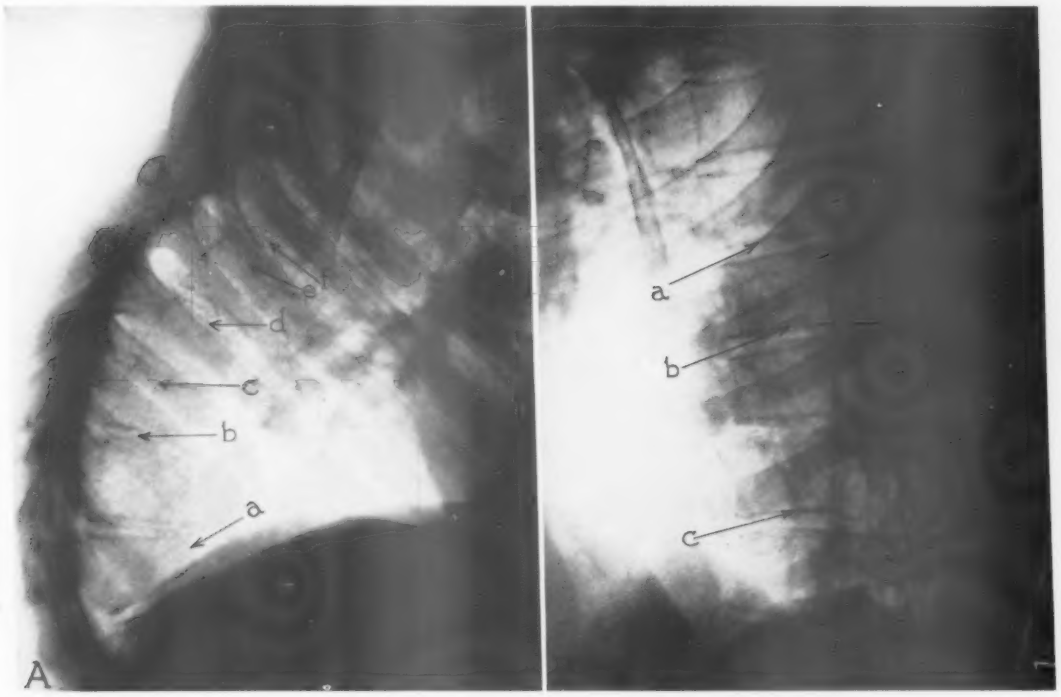


Fig. 17. Case VIII. *A*. Extreme degree of dorsum rotundum is well illustrated in this roentgenogram. The 12th thoracic vertebra is definitely wedge shaped (*a*) so that the height of the anterior portion is only about half that of the posterior part of the body. The irregularity of the articular portions of almost all of the vertebrae is noted and there are numerous punched out areas suggesting breaks in the cartilage plates and prolapse of the nuclei pulposi (*b.c.d.e.f.*). This patient was placed in a hyperextension turnbuckle plaster cast devised in this clinic for such corrections and a satisfactory degree of correction of the kyphosis was obtained (*B*). The spine was then fused by means of two full thickness tibial grafts (*d*). The intervertebral spaces were all appreciably widened by the correction of the spine so that erosion of the anterior portions of the vertebral bodies is no longer noted. Several punched out sclerosed areas (*a, b, c*) are now well demonstrated.

Roentgen Findings. The roentgen examination of July 10, 1930, revealed such a rounded kyphosis in the region of the lower dorsal spine

that it was not possible to correctly visualize the entire spine in the anteroposterior plates without making multiple repeated exposures. In the lateral view the 12th thoracic vertebra was distinctly wedge shaped, suggesting an old

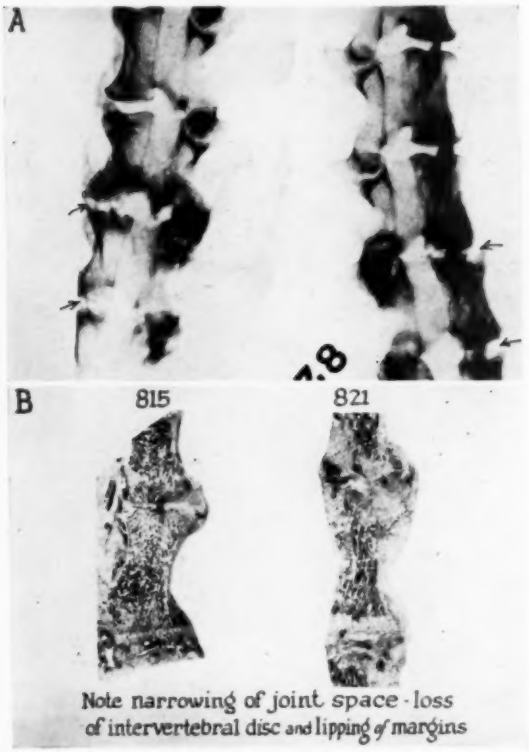


FIG. 18. *A.* Roentgenograms of the specimen of a dog's spine three months after the nuclei pulposi were curetted from two of the intervertebral discs. The wound was slightly infected but healed within four weeks. There is marked increased density of adjacent portions of the vertebral bodies, narrowing of the intervertebral spaces, irregularity of the articular surfaces, and lipping as indicated by the arrows. *B.* Reduced photomicrographs of sections of spines of two dogs subjected to the same type of experimental program as was described for *A*.

compression fracture and recalling the history of injury five years before coming to the clinic. In all views of the spine the articular surfaces of the vertebral bodies were rough and irregular with numerous punched out areas typical of prolapses of the nuclei pulposi. The intervertebral spaces were definitely narrow, especially in the thoracic region (Fig. 16).

On May 25, 1932, the roentgen examination revealed very marked increase in the kyphosis and an apparent decrease in the intervertebral spaces throughout the length of the spine. The anterior edges of each two vertebrae showed slight sclerosis and beginning lipping, due to the close approximation of adjacent surfaces and increased load at those points because of shifting backwards of the axis of motion from the damaged intervertebral discs to the posterior articular facettes (Fig. 17).

Comment. This patient was placed in a hyperextension turnbuckle cast, which was devised for and used successfully in similar cases in this clinic, and the kyphosis was partially corrected. The entire dorsal and upper two lumbar vertebrae were then arthrodesed by double full thickness tibial bone grafts. Immediately after beginning the hyperextension the pain in the back as well as the intercostal pain was relieved. The postoperative, hyperextension cast will be worn for another two months.

Discussion. The etiology in the production of the deformity in this case cannot be clearly established. Since this patient suffered from some back disability when she was eighteen or nineteen years of age we were at first led to make a diagnosis of epiphysitis dorsalis juvenilis. The roentgen examinations did not support this hypothesis. The punched out areas in the vertebral bodies were more centrally located and epiphyseal portions of the vertebral bodies were not definitely involved. The wedge-shaped compression of the 12th thoracic vertebra was certainly a factor in producing the deformity, but the extreme dorsum rotundum of all of the dorsal spine could not be explained on the basis of an injury to this one vertebra. It is our belief that this patient had numerous ruptures of the cartilaginous plates and prolapses of nucleus pulposus material. This may have been due in part to congenital defects at the site of the old notochord and such a condition would be further increased by trauma such as the patient experienced when she was run over by an automobile. If the wedge-shaped 12th thoracic vertebra did result from a compression fracture this was merely one more factor in producing the final extreme deformity. With the loss of nucleus pulposus material the intervertebral discs became more and more nar-

row until their function was reduced to that of a fibrous washer and the stress and irritation of the vertebral bodies, particularly where the weight was felt most severely, at the anterior edges, led to sclerosis, eburnation, beginning lipping, and irritation of the adjacent spinal nerves.

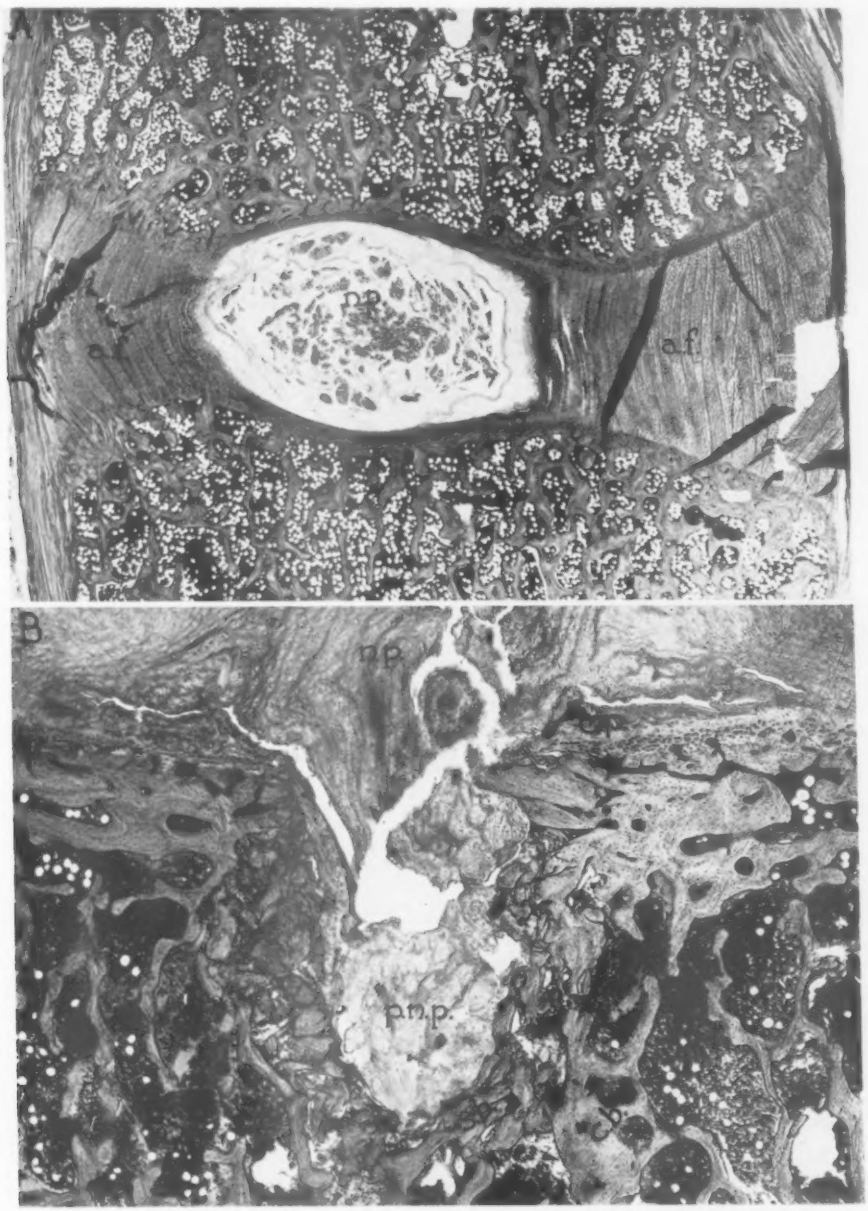


Fig. 19. A normal intervertebral disc of a dog is demonstrated in *A*. *n.p.*—nucleus pulposus; *a.f.*—annulus fibrosus; *c.p.*—cartilage plate; *c.b.*—cancellous bone of the vertebral body.

In *B* the cartilage plate of the intervertebral disc of a dog was injured with a small drill. A prolapse of the nucleus pulposus (*n.p.*) into the cancellous bone has formed a typical Schmorl cartilaginous nodule (*p.m.p.*) surrounded by a zone of sclerotic bone (*s.b.*).

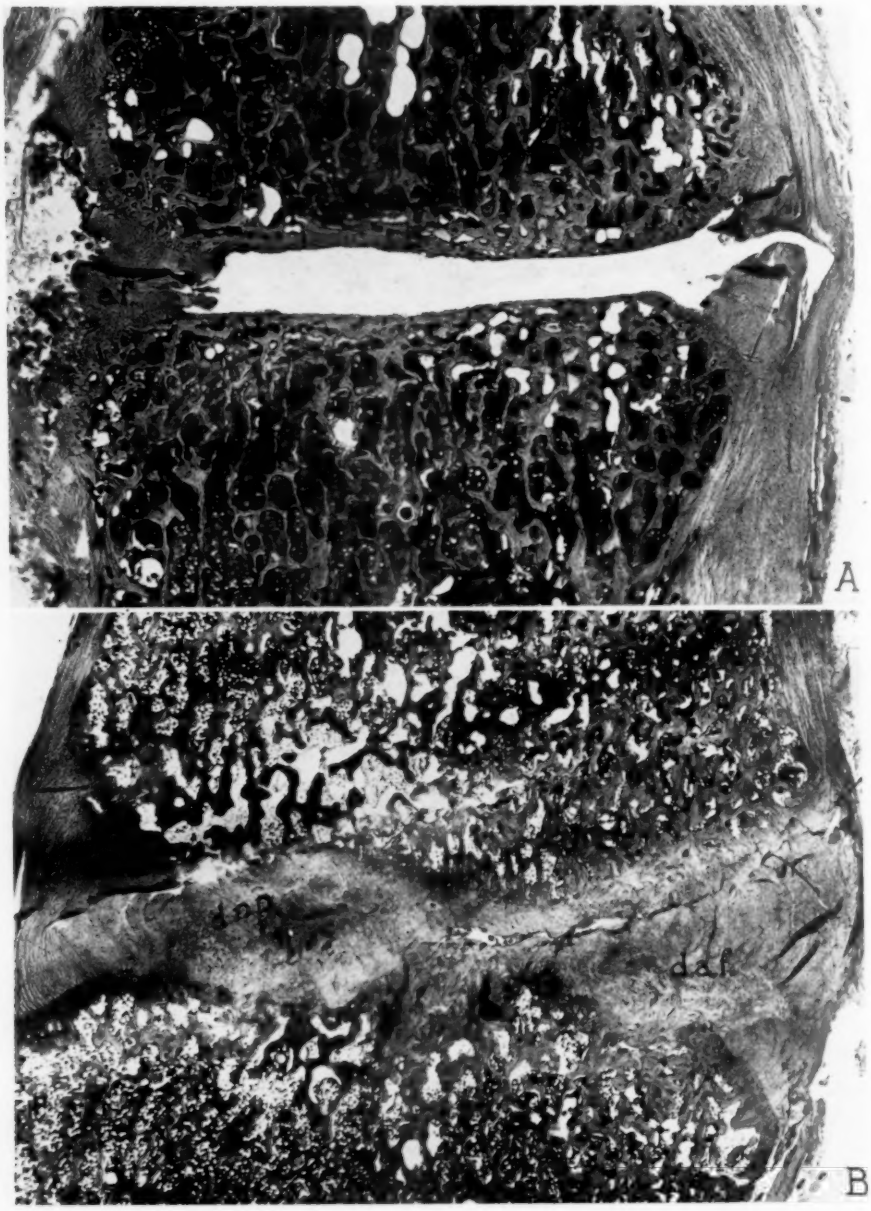


FIG. 20. In each of the photomicrographs of sections of spines of dogs in which the intervertebral disc was injured by incising the anterior fibers of the annulus fibrosus (*a.f.*) nucleus pulposus material was permitted to escape. The first specimen (*A*) was taken from a dog that survived less than three weeks after operation. The nucleus pulposus, cartilage plates, and most of the annulus fibrosus have been lost and the cortical bone is beginning to become sclerotic.

Less of the nucleus pulposus was removed from the disc (*B*). This dog was sacrificed after three months. There is typical degeneration and fibrosis of the remaining nucleus pulposus (*d.n.p.*) and annulus fibrosus (*d.a.f.*). The cartilage plate also shows degeneration, while sclerosis of bone extends deep into the cancellous portion of the vertebral body. Anteriorly there is beginning osteophyte formation.

EXPERIMENTAL STUDIES OF THE INTERVERTEBRAL DISC

Few reports of experimental studies of the intervertebral disc are to be found in the literature. Ribbert[23] in 1895 was able to produce a typical Virchow tumor by puncturing the intervertebral ligament and permitting a portion of the nucleus pulposus to escape. This material lying in the tissue formed a characteristic cartilage nodule which he called a chordoma. Roux[24] has studied the effect of pressure on the intervertebral disc and the vertebrae themselves. Püschel[21] estimated the water content of a series of normal and degenerated intervertebral discs in the various age-periods. We have repeated and confirmed this work.[12] Geist[10] and Petter[20] have studied the internal pressure of the intervertebral disc.

We have studied the effect of trauma to the vertebral bodies and the intervertebral discs. Dogs were used in most of the experiments. By means of chisels, drills or scalpels the vertebral body, cartilage plate or annulus fibrosus was injured. The animals were permitted to recover and were studied over a period of from two to six months before they were sacrificed.

In two dogs, in which the vertebral bodies were exposed by a paravertebral incision in the lumbar region and the intervertebral disc was opened with a small knife and the nuclear material was curetted out, there was a mild infection which persisted for from two to three weeks. In subsequent roentgen examinations (Fig. 18) the intervertebral discs were found to have completely disappeared and the adjacent bone surfaces became markedly sclerosed with spur formation and lipping of the anterior edges. These dogs developed a definite kyphosis. They were sacrificed three months after operation and the spines were sectioned and studied microscopically. The discs at the site of injury had disappeared, the bone was dense and there was marked hyperostosis and new bone formation very similar to that observed clinically in cases of marked osteoarthritis of the spine.

In the series of animals in which small drill holes were made through the cartilage plates, nuclear prolapses typical of the cartilage nodules described by Schmorl were found. All of these animals were sacrificed before sufficient time had elapsed to permit any marked bone sclerosis about the extruded nucleus pulposus material (Fig. 19).

Similar cartilage nodules were found extending into the cracks in the cartilage plates created by the chisel with which the vertebral bodies were fractured. In those vertebrae where the cartilage plate was not injured by the chisel, but merely the bone fractured, no prolapses were found.

In every instance where nucleus pulposus material had been permitted to escape, there was definite narrowing of the intervertebral disc and, when most of the nucleus was curetted out, the adjacent vertebrae showed early changes of typical hypertrophic or osteoarthritis of the spine and fibrosis of the material remaining in the space previously occupied by the nucleus pulposus (Fig. 20).

SUMMARY

The intervertebral discs are placed between each two vertebral bodies as shock absorbers which diminish the jarring effects of walking, running and jumping. The nucleus pulposus, although genetically derived from the notochord, is not a vestigial remnant, but a living and essential anatomical entity. It acts as a hydrodynamic ball bearing and axis of motion. Injury to the nucleus pulposus, either primary or secondary to injury or to disease of the adjacent vertebral body, cartilage plate or annulus fibrosus, results in a decrease in the normal function of the spine. The degree of disturbance in the function of the spine depends to a large extent upon the amount of substance lost from the nucleus pulposus.

Loss of nucleus pulposus material as a result of trauma or disease is probably one of the frequent etiological factors associ-

ated with pain in the back and disability. Lesions of this type can frequently be demonstrated in the roentgenographic studies.

Clinical, roentgenological, and experimental evidence has been presented to indicate that degenerative or hypertrophic arthritis of the spine may result from the loss of the nucleus pulposus with subsequent erosion and narrowing of the fibrous and cartilaginous portion of the intervertebral disc.

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DISCUSSION OF PAPERS BY DRS. GHORMLEY, PHEMISTER AND HATCHER, POMERANZ, HARBIN, RIGLER, AND COMPERE AND KEYES

DR. F. C. KIDNER, Detroit, Mich. I am greatly honored by the invitation to take part in this unusually interesting and valuable program. I also want to take this opportunity as an orthopedic surgeon to bear witness to the fact that my x-ray colleagues in this town make the practice of my specialty possible. They keep me awake by constantly presenting me with things that I don't know anything about, and I enjoy their company enormously.

Anything like an adequate discussion of this group of very able papers is, of course, impossible in the time allotted, but there are a few points on which I venture to comment. Dr. Ghormley's insistence on the necessity of familiarity with the gross pathology of joints as a prerequisite to the understanding of the x-ray shadow cannot be taken too seriously. We all realize the necessity of such familiarity but, unfortunately, too many of us ignore it in practice.

At the risk of lesé majesté, I am compelled to join issue with Dr. Phemister's statement that primary osseous tuberculous involvement of bone in children is usually in the metaphysis and that epiphyseal involvement is comparatively rare. Dr. Phemister's deserved reputation as an expert bone pathologist makes me fear greatly to disagree with him, but my experience over a long period at our Children's Hospital has seemed to demonstrate the reverse to be true. Perhaps in Chicago the action of Koch's bacillus is different from its action in Detroit. I am sure its actions in England and Switzerland are different from those in the United States. Otherwise the large percentage of recovery from joint tuberculosis with useful motion reported by those countries would be impossible. This I believe I have more or less proved by the many cases I have explored whose roentgenograms showed apparent bone focus in the epiphysis and when they were explored by operation showed little or no involvement of the synovia, no granulation tissue, and no inflammatory reaction in the synovia itself; therefore, I believe because of the later development in the cases that we really were dealing with tuberculous foci in the epiphysis. It may be merely a matter of coincidence that I have seen more epiphyseal tuberculosis and he more metaphyseal.

Until the last few years I have agreed with Dr. Pomeranz's attitude toward the early diagnosis of tubercluosis and the reliability of the x-ray in that diagnosis. Unfortunately, my faith has been shaken of late by too large a series of biopsies which contradicted roentgenograms interpreted by the best authority. Bone sclerosis early means some other disease.

I wish now to show four slides which present the knees of two individuals who suffered from a subacute, monarticular arthritis, practically identical in clinical course and symptoms and in pathological findings. One patient was an

overdeveloped boy of fifteen, the other a girl of twenty-three. Each had suffered one or more previous attacks of severe swelling of the affected knee with an unusual amount of pain. The attacks had come on following slight injuries, but without history of acute infection. The present attack in both cases had persisted in spite of good conservative treatment over a period of many weeks. It had been accompanied by fever up to 100.5°F., a moderate leucocytosis not above 10,000, with a moderate increase of polymorphonuclear cells. The pain was the most pronounced symptom and was very severe, requiring much morphine in spite of plaster fixation. Both knees had been tapped by the family physicians in their home towns, and cultures in both cases were said to have been positive for streptococci. The fluids which I withdrew was in both cases sterile, but so full of leucocytes it resembled pus.

Exploratory operation was finally undertaken for diagnosis, and if possible to save knee function. In both cases an enormously edematous synovia more than half an inch thick was found. On the theory that removal of the synovia might remove the cause of the symptoms, complete synovectomy was done in both cases. In the boy, fever and leucocytosis disappeared on the third day, and pain on the second day. After two weeks of complete rest motion was started in the knee, and now, at the end of three months, he has 60 per cent normal motion and no symptoms. The girl had a mild postoperative infection with *S. albus*, which cleared up promptly and she is now regaining motion.

Pathological examination of the tissues removed at operation showed no bacteria, and cultures on many kinds of media produced no growth. The synovia on section showed a marked plasma cell infiltration.

In a recent number of *Archives of Surgery*, Dr. Smith, of the New York Orthopaedic Hospital, reported a number of cases similar to these two, for which he gave no explanation but emphasized the danger of confusing them with tuberculosis. Our pathologist at the hospital has suggested that they might be due to *Brucella abortus*.

(Slide) This is the case of the boy. Unfortunately the x-rays, taken in the country, were not centered, but I think you can see there is nothing wrong with the bone, but that the synovia is thickened and the suprapatellar pouch swollen.

(Slide) Here he is after the synovectomy. and even this evidence is lacking in the spine There is apparently still no destruction whatever of the cartilage in the joint; a perfectly normal looking joint surface, but a considerable absorption of calcium which might suggest the early stages of tuberculosis.

(Slide) Here is the girl before the operation. At this point—I did not discover this, but Dr. Evans pointed it out to me—there is subcartilaginous absorption of the bone which might resemble the appearances of early tuberculosis.

(Slide) The next picture taken after the secondary infection, six weeks after the original operation shows very marked fuzziness of the cartilage and thickening of the capsule, which might again easily be translated as the early stages of tuberculosis, but is rather disproved by the fact that we have had very thorough biopsy of this enormous amount of excised material and found no tuberculosis.

I present those two cases merely to accent the fact that although the x-ray has gone a long, long way in diagnosis we still have to depend on the clinical findings and on pathological sections removed from the joint. In this connection I want to thank Dr. Harbin for emphasizing the necessity of exploration of the osteochondritis cases. I think we will never get anywhere until we do explore cases and take out specimens.

DR. C. A. WATERS, Baltimore. A discussion of the splendid papers which we have just heard might well be confined to an expression of thanks to the authors for such an illuminating presentation of the changes in bone and joint disease. I can say little which is not already familiar to you. Yet, the confusion which exists with regard to joint changes, especially the arthritides, prompts me to make a few remarks as to the formulation of a simple roentgen classification which, I believe, is satisfactory. I can well remember the time when it was thought possible to differentiate the etiological factors underlying the various types of arthritis; the development of a healthful conservatism has rendered such differentiation less evident and now the great majority of cases of arthritis may be divided simply into atrophic and hypertrophic groups. The pathological changes and the stage of the disease at the time of examination obviously determine the roentgen findings. For example, the classical painful, red, swollen, hot joint which is seen soon after any localized physical insult will give roentgen evidence of its state only in the form of edema,

and temporomandibular regions. It is not until actual destruction or proliferation of tissues occurs that one can distinguish between the different forms of arthritis. It seems to me that a grouping on a basis of destructive changes, on the one hand, and proliferative changes, on the other, is most satisfactory. The first group we refer to as the infectious and atrophic type; the latter as the hypertrophic type. The differentiating criteria consist in:

Atrophic Type (Infectious)

1. Marked destruction of the articular surfaces with marked narrowing of the interarticular space.
2. Decalcification of the bones.
3. Little or no new bone formation.
4. Terminal fibrous ankylosis.

Hypertrophic Type

1. Very little destruction of the articular surfaces with less marked narrowing of the interarticular space.
2. No decalcification. On the other hand, bones often increased in density.
3. Marked new bone formation.
4. Little tendency to ankylosis.

When one considers the forms of specific arthritis, I think it can truthfully be said that tuberculosis can be distinguished from the evidence on the film.

In closing, I would like to say that the term "traumatic arthritis" is one which I think should be used with extreme caution, if at all, for the door is here opened to medicolegal action where it might otherwise be somewhat less ajar. Time after time we are being called into court to testify as to the existence of a "traumatic arthritis" and nearly always these patients have had a hypertrophic arthritis of long duration which has been painfully brought to the patient's attention as a result of the injury.

Dr. G. E. Pfahler, Philadelphia. I should like to ask whether anyone has recognized any x-ray characteristic of gonorrheal arthritis.

Dr. M. C. Sosman, Boston. I recently had the privilege of hearing a noted pathologist, Dr. Pick, of Berlin, talk on the same subject Dr. Harbin presented so well. Dr. Pick promoted the theory that these changes are aseptic subchondral necroses due to small infarcts of the terminal arteries. I should like to ask Dr. Harbin if he will comment on that theory.

Dr. Ghormley (*closing*). I don't believe a typical picture of gonorrheal arthritis exists, from the pathologic standpoint at least, for the same picture may be seen in other types of arthritis. One can guess that a certain roentgenographic picture is that of gonorrheal arthritis, and one may be right, but in a great many cases, wrong. Tuberculosis occupies the attention more often than any other condition when speaking of roentgenographic changes, and my feeling is that in interpreting the roentgenogram, if changes are present, one can often make a positive diagnosis, but it is not fair to the patient, the clinician, or the roentgenologist to make that diagnosis too positive. The only final decision concerning tuberculosis should rest on biopsy, in which case one can be pretty sure of the diagnosis. In the series of more than 120 dissected joints that we studied at The Mayo Clinic, we found that from biopsy we were able to make a correct diagnosis in all but 3 per cent of the cases, and that far outnumbered the correct findings from any other source of diagnosis.

Dr. Phemister (*closing*). In reply to Dr. Kidner I only want to reiterate that where the lesion of the bone is sufficiently large and the changes in the articular surfaces are sufficiently early for us to feel that the condition was primarily osseous, in our experience it has been more frequently in the metaphysis than in the epiphysis. I want to emphasize the other point, that the supposedly primary lesion in the bone, with extensive destruction and breaking down in the weight-bearing portions, is usually secondary instead of primary, as shown by the bilateral involvement.

Dr. Harbin (*closing*). In regard to Dr. Sosman's question concerning aseptic necrosis as related to osteochondritis, I think that is a relatively old theory. I know when we were investigating this disease some four or five years ago it was frequently considered as a possibility but lacked sufficient proof to be generally accepted. I do not believe as yet there is any definite knowledge as to etiology. I know that we have all thought of a number of possible etiological factors. A great many of us have tried to produce the disease experimentally, and all have failed, with the exception of Mau, who feels that he has produced osteochondritis in the tail of the rat, beyond this I am not familiar with any experimental proof. In the early days we thought of infection as a strong probability, but in the majority of our cases in which we have done biopsies we have obtained sterile cultures, and are beginning to feel that the few cases in which positive cultures have occurred, the organisms may have been present without actually being responsible for the pathology.

ROENTGENOGRAPHIC INVESTIGATION OF THE TIME ELEMENT IN OSSIFICATION

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Shortly after the announcement of the discovery of X-rays in 1895, I thought I saw an opportunity of using this method in a research, corroborating or correcting the time element in commencing ossification as given in the standard works of anatomy. It was not, however, until 1905 that I had collected sufficient data on which to base an opinion. I then published a brief account of my findings. This method seemed to me to be the only one in which a large number of subjects could be obtained, and the average time at which the centres of ossification were making their appearance determined with accuracy. In using living material for this examination a subject of desired age could be selected and could be subsequently re-examined for months, or even years as the results indicated. The rate of growth could thus be determined while in other subjects the times of appearance of centres of ossification could be estimated with reasonable accuracy.

I AM quoting the above from an article I read before the Anatomical Society of Great Britain and Ireland in London on November 28, 1927, and published in the *British Journal of Anatomy*, July, 1928. I also read this paper before the Anatomical Society of the Ecole de Médécine in Paris on December 1, 1927. I am giving this quotation for the reason that I want to call attention to my conclusions published from 1905 to 1925, and the corroboration of these findings by a large number of investigators.

I am giving special emphasis to the determining of sex by this method.

Hess (1917) used this method in determining the age of the fetus but did not differentiate the sex. He says:

> The determination of the age of the fetus is of considerable practical importance. On the age of the fetus and on its development are based the chief factors that are to be considered before giving prognosis as to the possibility of saving the life of the prematurely born infant. . . . In medicolegal cases the question of the age of the fetus may occasionally be of paramount importance, and when only portions of the fetus are available for examination, the roentgenographic method offers the best means for arriving at a diagnosis of the age of such fetus.
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> The peculiar advantage of the roentgenographic method for determining the age of the fetus lies in the fact that while in the determination of age according to the length we base our final conclusions usually on one, rarely on two or three measurements expressing different lengths of the fetus, in the roentgenographic method many centers of ossification are the factors taken into consideration before arriving at a final conclusion; and they act as check on each other and quite frequently the roentgenograms alone give us information as to whether the fetus is normal or not, a point which seldom may be determined from measurements alone.
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> . . . . . .

His conclusions are:

1. The stage of ossification of the skeleton of the fetus as observed in roentgenograms is of considerable practical importance in determining the age of the fetus.
2. The roentgenographic method of determining the age of the fetus is more reliable than determination of age based on length and other measurements, since osseous development is more regular and offers many more factors for consideration; one part of the body is a criterion of normality for the other parts, and pathology may often be readily recognized.
3. In the early months more accurate determination is possible than in the later months, and the roentgenographic method is undoubtedly capable of much greater refinement by further studies and observations.

My first conclusions (1905) were given in the form of a summary as follows:

Carpus	Os Magnum	*Female:* between the third and fourth month. *Male:* between the seventh and eighth month.
	Unciform	*Female:* between the third and fourth month. *Male:* between the seventh and eighth month.
	Cuneiform	*Female:* thirteenth or fourteenth month. *Male:* early in the third year.
	Semilunar	*Female:* late in third or early in fourth year. *Male:* between the fourth and fifth year.
	Scaphoid	*Female:* when about four years of age. *Male:* when about six years of age.
	Trapezoid	*Female:* between the fourth and fifth year. *Male:* between the fifth and sixth year.
	Trapezium	*Female:* between the fourth and fifth year (usually preceded by the trapezoid). *Male:* early in the eighth year (usually preceded by the trapezoid.)
	Pisiform	*Female:* between the ninth and tenth year. *Male:* between the twelfth and thirteenth year.
Metacarpus	Epiphyses	*Female:* index, middle, ring and little fingers, successively, at distal end, the first named appearing about the tenth month, the last during the fifteenth month; that at proximal end of a thumb at two and one-half years. They unite with the shaft in the sixteenth year. *Male:* not determined; certainly several months later. They unite with the shaft during the eighteenth year.
Phalanges	Epiphyses	*Female:* first row; index, ring and little fingers, successively, the first named appears from the eighth to the twelfth month, the last named from the twelfth to the fifteenth month. Second row: middle, ring and index fingers, appears from the eleventh to the fifteenth month. Last row: or ungual phalanx of the middle, ring and thumb, appears from the fourteenth to the eighteenth month. The first phalanx of thumb and the second of the little finger appears when between two and three years of age. The ungual phalanx of index and little fingers, appears a few months later. They are all united with the shaft by the end of the sixteenth year. *Male:* not determined; certainly several months later. They unite with the shaft during the eighteenth year.
Radius	Epiphysis	*Female:* appears about the eighth month. *Male:* appears early in the second year.
Ulna	Epiphysis	*Female:* appears between sixth and seventh year. *Male:* appears between seventh and eighth year.

In subsequent years I have made a few changes in the above table; notably the appearance of centers of ossification in the epiphyses and their union with the diaphyses.

In corroboration of these findings, I quote the following:

In 1921 Dr. Arthur Grumbach published the result of his study of 800 hands; mostly adults. He refers to Quain and Pryor as chief authorities on the question of carpal ossification with respect to the time and order of ossification.

Carter (1923) says:

The first systematic and rather elaborate study of the ossification process in the hands of young children seems to have been made by Dr. J. W. Pryor of the University of Kentucky. The study began in 1906 and was carried on over a period of several years. More than five hundred children were included in the study, most of whom were under seven years of age.

I give the following from Hess and Weinstock:

During the last few years, studies of the development of the carpal centers of children have been numerous. To this end roentgenograms have been employed and have been the means of providing much more reliable and valuable information than the old anatomic method.

In many of these inquiries the factor of sex is not taken into consideration. The data of the more important of these studies are reproduced in tabular form in a recent article by Scammon. *As he states the most satisfactory investigation is that of Pryor which was carried out on American children and for this very reason has additional value for us. Pryor recognized the fact that the female infant is relatively precocious* in its development of carpal centers; that whether we regard the question from the point of view of relative age or of length, the female baby develops these centers at an earlier period than the male.

Dorland and Hubeny (1926) have corroborated my findings as follows:

The *os magnum* (*os capitatum*) is the first bone in the human carpus to begin the process of ossification. In the female hand, the center appears before the child is six months old. In exceptional instances, ossification may begin before birth. The average appearance of this center is between the third and sixth month after birth, and that for the *unciform* (*os hamatum*) a few months later. The *cuneiform* center will make its appearance between the second and third year. The fourth bone of the carpus to begin ossification is the *semilunar*, the nucleus of which will appear between the third and fourth year; while that of the *scaphoid* will appear when the child is about four years of age or early in the fifth year. It is only in rare or exceptional cases that the semilunar or scaphoid centers will appear after the child is five years of age. The *trapezoid* and *trapezium* nuclei will make their appearance between the fourth and fifth years in the order named. The last bone, the *pisiform*, will begin ossification between the ninth and tenth years.

The following quotation is from my publication of 1908:

The carpal development may be tabulated as follows:

Os magnum —Female, between third and sixth month; male, between fourth and tenth month.

Unciform —Female, between fifth and tenth month; male, between sixth and twelfth month.

Cuneiform —Female, between second and third year; male, when about three years of age.

Semilunar —Female, between third and fourth year; male, when about four years of age.

Scaphoid —Female, at four years of age or early in the fifth year; male, when about five years of age.

Trapezoid —Female, between fourth and fifth year (preceding the trapezium); male, between fifth and sixth year (preceded by the trapezium).

Trapezium —Female, between fourth and fifth year (preceded by the trapezoid); male, between fifth and sixth year (preceding the trapezoid).

Pisiform —Female, between ninth and tenth year; male, between twelfth and thirteenth year.

The bones of the female carpus ossify in advance of those of the male carpus; this is measured at first by days, then months, then years. The chronologic order in which the bones of the carpus are ossified differs from that formerly supposed. The larger size of the nucleus does not always signify priority of appearance. In all the bones of the carpus the first appearance of the center is that of a pin-point. This becomes round, then elongated, and as it enlarges the shadow assumes the characteristic of each bone. Thus, that of the os magnum is longer in the vertical diameter and is usually constricted in the middle. The unciform always assumes a triangular shape, with the apex toward the center and directed obliquely downward and inward. The cuneiform becomes oval with the long diameter running obliquely downward and inward. The semilunar remains round generally, but often becomes pyramidal. The scaphoid rapidly grows in the long diameter of the bone and soon distinctly anticipates the boat-shape. The trapezoid and trapezium remain round until they are quite large.

A pertinent question arises as to the reason why ossification occurs earlier in the female than in the male. It is probable that an explanation of this interesting fact will be found in the greater and earlier hormonic action in girls than in boys. Anatomically, girls mature faster than boys.

The usual order of ossification of the bones of the carpus, as determined by the X-ray, is: 1. Os magnum; 2. Unciform; 3. Cuneiform; 4. Semilunar; 5. Scaphoid; 6. Trapezoid; 7. Trapezium; 8. Pisiform. The bones of the first child, as a rule, but not invariably, ossify

sooner than those of subsequent children (Pryor). The ossification is bilaterally symmetric. The ossification of the epiphyses of the bones of the hand, as determined by Pryor, is given in the accompanying Table.

A more striking corroboration of my findings is given by Paterson (1929). I am calling special attention to his conclusions in regard to the union of the epiphyses.

The Hand and Wrist

This section includes the lower end of the radius and ulna, the carpus, metacarpals, and the phalanges. A comparison of the dates given by various authors will be found in the tables in Appendix I.

Frazer described a separate centre for the styloid process of the ulna, but apart from trauma no specimen of this condition was discovered, nor could any evidence be traced of a separate centre for the tubercle of the radius which he mentions as occurring about twenty and joining a few years later.

Phalanges

The epiphyses occur at the proximal end of the phalanges and for practical purposes they seem to appear simultaneously in all three rows. The date of their appearance is relatively constant and was found to be during the third year in males and during the second year in females. *No cases were observed of the epiphyses occurring before the third year in males but in all the female cases it was present in the second year.* They joined their diaphyses in the male group at the age of nineteen, and in females at seventeen.

Metacarpals

The epiphyses for the metacarpals occur at their distal ends with the exception of that at the first which is at the proximal end. The date of their appearance is the same as those of the phalanges, i.e., males third year, females second year. The epiphysis of the first metacarpal appears generally somewhat later than the others—up to six months later. Dates of joining the epiphyses were as follows:

	% 15 yrs.	% 16 yrs.	% 17 yrs.	% 18 yrs.	% 19 yrs.
Males	0	4	15	55	82
Females	32	50	100	—	—

The average age at which the epiphyses of the phalanges and metacarpals join their diaphyses may therefore be stated to be nineteen in males and seventeen in females.

Double epiphyses (proximal and distal) on some or all of the phalanges and metacarpals occurred in several cases. In one of them which was investigated they were apparently hereditary, occurring in the father and two children. These have been described as "pseudo epiphyses" and are not uncommon, sometimes being completely separate and sometimes partially or almost completely fused.

In the present series there were eight cases of double epiphyses, five of them however were confined to the first metacarpal. As far as could be ascertained, these cases were present in perfectly normal individuals.

The Carpus

All the bones of the carpus normally ossify from a single centre. A double centre for the cuneiform has been described by Pfitzner. It is exceedingly rare and no case of double ossific centres was present in this series. There is a considerable variation in the size and shape of the carpal bones in different individuals. The order of the appearance of the centres was found in males to be under:

Os magnum. Appears during the first six months after birth.

Unciform. Also appears before six months. The widest variations in these bones are from one to six months.

Cuneiform. End of third year and beginning of fourth. In no case was it present before the beginning of the third year and in only one case was it not present until the fifth year.

Semilunar. End of fourth year or early in the fifth year and the variation limits were between these dates.

Trapezium and trapezoid. Appeared very constantly in the sixth year. There was not more than a six-months variation each way.

Scaphoid. This bone also appeared during the sixth year—see note later.

Pisiform. This is the most variable of the carpal bones; the figures were as follows: 25 per cent at eleven years, 55 per cent at twelve years, 80 per cent at thirteen years, and was present in all cases at fourteen years old. This epiphysis frequently had a "fuzzy" or crumbled appearance which however does not appear to be of any significance.

The figures for female children differ slightly from the above and work out as follows:

Os magnum. Always present at six months.

Unciform. Always present at six months.

Cuneiform. End of second year and beginning of third.

Semilunar. In 50 per cent of cases was visible during the third year and was invariably present in the fourth year.

Trapezium and trapezoid. End of fourth and beginning of fifth year.

Scaphoid. During fourth year.

Pisiform. Present usually in ninth year, always present in tenth. This carpal bone was in several instances present at the eighth year.

The order of appearance of the trapezium, trapezoid and scaphoid is subject to variation, the two former sometimes appearing before the scaphoid and sometimes after it. It would appear therefore that the *centres for the carpus appear from one to two years earlier in females*, except the pisiform which may be *three or four years earlier*. Frazer states: "Ossification of epiphyses appears to start about a year earlier in females in the metacarpus and phalanges and in them the fusion with the shaft is also earlier, in male bones it occurs about eighteen to twenty."

. . . . . .

Conclusions

Several conclusions, it would appear, are to be drawn from the foregoing investigations. *A most striking feature is the difference in the times of appearance, and more particularly in the times of the union of the epiphyses of the two sexes*. This difference has been pointed out before but has not been stressed in proportion to its importance, and although the bare fact of the existence of a difference has been quoted by many authors, few actual figures were found in the literature. It is seen that in the case, for instance, of the epiphyses around the elbow joint, there exists a difference of four years between the average dates of union in the two sexes. Parsons and Davies, in a series of epiphyses examined radiographically, also found the dates earlier in females than in males. It is evident, therefore, that any estimation or investigation of these dates, where a sex differentiation has not been made, will give a varying date. If the series contains a preponderance of males, then the date will be a comparatively late one, and if conversely the series predominates in female specimens, it will give a relatively early date of union. It seems possible that this fact may have given rise to some of the very wide ranges of time that have been assigned to various joints, such as "eighteen to twenty-two," and in addition may also account for the wide variations given by authorities for the same epiphyses.

The sex difference in epiphyseal ossification is becoming more recognized. Adair and Scammon have shown that the same relationship holds in intrauterine ossification, and that in the fetus ossification proceeds more rapidly in females even though their weight and dimensions are less than those of males. The older the individual the more marked is the difference between the two sexes as regards their epiphyses, so that the disparity in the dates of fusion is greater than that of the dates of appearance. As Pryor expresses it: "The bones of the female ossify in advance of the male. This is measured at first by days, then months, then years."

I have given this extensive quotation from Paterson as it verifies all of my conclusions made from 1905 to 1923.

A still more recent publication is that of Sawtell (1929). She says:

> The pioneer study of joints by roentgen-ray pictures, that of Poland, dealt exclusively with the wrist and hand. Then in 1905 and 1908, Pryor and Rotch began their long series of publications devoted to the ossification and development of the wrist and the grading of roentgenograms.
>
> Both men used the method of inspection alone. But whereas Rotch eliminated age and sex and classified roentgenograms only on the basis of carpal development, with the head of metacarpals and phalanges as controls in three of his thirteen groups, *Pryor continually emphasized the marked acceleration of the female in development for the centers in the carpus and the epiphyses of the hand, from appearance in the embryo to union with diaphyses after puberty*.

It would seem from the conclusions of these various investigators, that the sex difference is an established fact. The difference in ossification in the embryo and fetus, that is, in prenatal life, is measured by days and weeks while that in postnatal life is that of months and years.

Hess states,

The stage of ossification of the skeleton of the fetus in roentgenograms is of considerable practical importance in determining the age of the fetus.

The same may be said of determining the sex of the fetus.

I have very little to illustrate this in prenatal life. The one I am calling to your attention is an embryo of a 52 mm. female.

This shows extensive ossification in the long bones, ribs, clavicle, mandible, maxilla and a large number of centers are seen in the vertebrae. The special point I would call to your attention is the ilium and ischium. Knowing the length and estimated age of this embryo it could be said to be female in perhaps 98 per cent of instances. I am supposing the external genitalia had been so mutilated that resort to the roentgenogram was necessary to determine the sex.

While the determination of sex by ossification may have very little practical value, in rare instances it may be of some medicolegal valuation.

These facts would bring up the question: Could the sex of the fetus *in utero* be determined by this method?

If it were possible to make roentgenograms showing the carpus, tarsus and the distal end of the femur with the central end of the tibia, a grouping of the centers at these points, if present or absent, would indicate the sex in many cases.

For instance, let us take the following illustration. This is a newborn infant of four days of age. There are centers of ossification in the capitate and the hamate of a size that would indicate ten days' to two weeks' growth. That of the talus and calcaneus shows several months' growth and that of the cuboid at least three weeks', while those of the femur and tibia show at least six weeks' growth. Had roentgenograms of this child been made a few weeks before birth, showing the stage of ossification, it could have been said positively to be female, and 100 per cent, for I do not believe a single male could be found showing this advanced condition of ossification.

Now let us take the negative side.

We will use No. 1 of my series, a male one day of age. The calcaneous is 6 mm., talus 5 mm., cuboid 0, femur 3 mm., and tibia 0 in size. No centers have appeared in the carpus. Had a roentgenogram of this child been taken *in utero* a week or two before birth, showing the stage of ossification, it could have been positively stated it was male.

These are the extremes and granting there are marked differences between the male and female skeleton, groupings can be made that will determine the sex in a large percentage. In early postnatal life, the problem is not so difficult. The illustration of M. B., one year, two months and twenty days, is one that could be pronounced female in 100 per cent of cases. I have never seen a male that could approach this advanced condition of ossification. From birth to eight or nine years of age the difference in ossification is so marked, a large percentage could be determined. From this period until the age of union of the epiphyses the problem is a very difficult one and without more data I would not be willing to express an opinion. From the age of fourteen to eighteen we have positive data that would determine the sex.

Where we find a union of the epiphyses in the phalanges and metacarpals at age fourteen to fifteen it will be found to be 100 per cent female.

The illustration I am calling attention to is a female fourteen years three months and twenty-one days of age in which all the epiphyses of the phalanges and metacarpals have united with the diaphyses.

Between the age of fifteen and sixteen the percentage would be 95 female if the union was complete and when we find the union of these epiphyses complete between the age of sixteen and seventeen we can safely say that 90 per cent will be female, and between the ages of seventeen and eighteen if these epiphyses are united it will be found that 85 per cent are female.

To some these facts will have no prac-

tical value whatever. I am not so sure of this; but they may lead to something in the future that will prove of value, and if not so practical, will at least have some bearing on scientific accuracy.

CONCLUSIONS

The differences in the ossification of the male and female skeleton is a proved fact.

In prenatal life it is measured by days and weeks.

In postnatal life it is measured by months and years.

The epiphyses of the long bones unite with the diaphyses in the female from two to four years sooner than in the male.

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PRIMARY CHONDROMA OF THE LUNG*

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THE appearance in this hospital of two further cases of primary chondroma of the lung has stimulated a review of the work of Hickey and Simpson,[2] and the available literature since their publication in 1926.

The majority of these tumors are located near the pleural surface. In a few cases they have been described as occurring between the pulmonary lobes. The neoplasm is usually round or oval, varies greatly in size, and is always encapsulated. Two characteristics, the nodular, lobulated structure, and the tendency to undergo calcification or osseous transformation are important from a roentgen standpoint.

Microscopically the most prominent element is cartilage; both the hyaline and the fibrous type are frequently encountered. The center of the tumor mass may show evidence of retrogression in the form of myxomatous degeneration or as liquefaction necrosis. Small calcium deposits, or islands of true bone which may contain bone marrow, are commonly scattered throughout the tumor. The connective tissue is often myxomatous while the septa and capsule are extremely vascular and of a rather embryonal character. Adipose tissue and smooth muscle bundles are intermixed in the connective tissue stroma. A most interesting feature is the occurrence of duct or bronchial-like structures lined with epithelium varying in type from simple cuboidal cells to ciliated cylindrical cells.

In the roentgenogram a primary pulmonary chondroma should present the following appearance: (1) An abnormal mass of great relative density surrounded by normal air-containing lung, (2) a sharply defined lobulated border, and (3) containing within it scattered, irregular areas of even greater density representing calcium or bone.

In the differential diagnosis, the sharply defined periphery of the chondroma surrounded by normally aerated lung is easily distinguished from an encapsulated chronic inflammation, such as an old abscess or tuberculous lesion with calcification. Cellular infiltration in the immediate lung parenchyma usually accompanies an inflammatory condition. It is absent in the neighborhood of the chondroma. Solitary echinococcus cysts of the lung occur more often than primary pulmonary chondroma. The roentgenographic appearance is similar. But the border of the shadow of the ecchinococcus cyst is smoother, and there may be slight cellular infiltration in the surrounding lung parenchyma. The cystic mass is usually of homogeneous density. The history of previous infestation with *Taenia ecchinococcus*, potential exposure to the parasite, and the complement fixation test are of value in making the differentiation.

Some authors have insisted that the tumor has no connection with the bronchi. Others have intimated an origin in bronchial cartilage. Hickey and Simpson (1926) summarized the information as follows: "It might be said that the so-called pulmonary chondroma probably represents a tumor having origin in aberrant bronchial anlagen, since all of the structures which go to make up these mixed tumors are normal components of the bronchi."

Vanzetti (1927) believed the tumor to be a relatively advanced disturbance in the bronchial system, an advanced embryonal rest.

Bayer (1929) believed that the tumor arises from the larger bronchi. This was assumed because of the bronchial type of

* From the Department of Roentgenology, University of Michigan, Ann Arbor. Read before the Detroit Roentgen Ray Society, May 26, 1932.

TABULATED ABSTRACTS OF REPORTED CASES SINCE 1926

NOTE: Cases 1 to 40 abstracted by Hickey and Simpson[2]

No.	Reference	Sex	Age	Gross Pathology	Microscopic Examination
41	Bayer[1]		81	Incarcerated femoral hernia. Pepper cone sized chondroma. *No mention of roentgen examination*	The cartilage has a fine, thready, ground substance. At the edges of the tumor mass it gradually changes to a fine, fibrous-like tissue. Some of these fibers take Weigert's elastic stain. Occasional fat cells are found in the cartilaginous borders. The nodules are separated by connective tissue. In this connective tissue are numerous, somewhat branching and saccular ducts lined by tall cylindrical cells and in part by ciliated columnar epithelium. Under the epithelium is a definite elastic membrane, often double. In between these epithelial structures are small veins, capillaries, fat cells, and here and there lymphoid tissue.
42	Bayer[1]	M	71	Hypertrophy of the prostate and pyelo-nephritis. Hazelnut sized chondroma in right lower lobe; 2 cm. beneath the visceral pleura. *No mention of roentgen examination*	Mass consists of hyaline cartilage showing a fibrous structure at a few points along its border. The cartilage is divided into islands by connective tissue septa. The remainder of the description is similar to Case 41 except that some of the ducts are partially filled with a collagenous material staining red with van Gieson's. Carbon-containing cells are scattered throughout the lymphatic tissue in the tumor.
43	Bayer[1]	M	57	Carcinoma of cardia of stomach; apical tuberculosis-chondroma in left lower lobe, subpleural, encapsulated, knotty, "stone hard." *No mention of roentgen examination*	The tumor consists of both hyaline and fibrocartilage. Similar to Cases 41 and 42 except for definite calcified areas in the cartilage. The epithelium of the ducts is less evident. Lymphoid tissue present in tumor.
44	Bayer[1]			Clinical data lacking. Walnut-sized chondroma in right upper lobe. Cut surface has a fine granular appearance. *No mention of roentgen extion*	Microscopic findings are essentially the same as Case 43. Lymphoid tissue is markedly increased in amount and there are bundles of smooth muscle in the walls of the larger ducts. These are lined with cylindrical epithelium.
45	Bayer[1]			Only section from tumor available. *No mention of roentgen examination*	Formation is similar to previous Cases 41 to 44. Numerous branching and sacculated ducts in connective tissue septa and capsule. These ducts are lined with cuboid to cylindrical type epithelium. Between the ducts are numerous small vessels, lymphoid tissue, and in some areas bundles of smooth muscle fibers.

No.	Reference	Sex	Age	Gross Pathology	Microscopic Examination
46	Klages[3]	F	29	History of severe coughing, hemoptysis; no tubercle bacilli; recovered slowly. *Roentgen examination demonstrated an ovoid tumor mass in the right lower lung 7×6 cm. in diameter. Areas of increased and decreased densities suggesting a knotty tumor containing calcium deposits. Diagnosis-pulmonary chondroma.* Operation—encapsulated tumor mass removed from right lower lobe, patient recovered rapidly. Living and well 2½ years later. *Recognized from roentgen appearance before operation.*	Microscopically the tumor is covered with a heavy connective tissue capsule, and divided by numerous connective tissue septa. The major portion of the tumor is cartilage—both fibroid and hyaline in type, containing some large but mostly small lacunae in which large oval nuclei are enmeshed in a fine protoplasmic ground substance. A gradual transition from cartilage to myxomatous tissue. There are typical star cells between fine reddish fibers in a fine gray-blue meshwork. A third substance—atypical bone tissue composed of a thick spongy stroma with heavy trabeculae and even-sized small bony corpuscles. The calcification is irregular and the bone marrow is of a fatty nature. The transitions between cartilaginous and bony structures of the tumor are gradual. Epithelial and endothelial elements are not found.
47	Paul[1]	M	69	Suffered with asthma since youth. Last illness lasted three months. Autopsy—polypoid chondroma with bronchiectasis, bronchostenosis, contraction of the left lung, empyema and thrombosis of the spleen. *No mention of roentgen examination*	The tumor is surrounded by bronchial epithelium and encapsulated by thick connective tissue. Septa divides the tumor into nodules. The cartilage show considerable myxomatous degeneration but contains areas of ossification. At the borders of the cartilaginous masses are ducts lined with simple cylindrical epithelium, some of which are filled with a mucoid substance. Elastic fibers, capillaries, fat cells, and lymphoid tissue are interspersed with the connective tissue septa and ducts.
48	Vanzetti[2]	M	41	Two chondromata. One in upper lobe and other in lower lobe, each about 16 mm. in diameter. *No mention of roentgen examination*	Cartilage of a fibro-elastic type predominates. Ducts lined with cylindrial epithelium, some with stratified epithelium. Have the same character as epithelium lining the small bronchioles. In the walls of the ducts are small bundles of smooth muscle. Elastic tissue, adipose tissue, and connective tissue are also found in the tumor.
49	Authors' Case No. 279994	M	30	Encapsulated tumor 6×6×5 cm. in diameter in right lower lobe, of rubbery consistency, with occasional lime salt deposits throughout the mass. *Tumor was discovered by roentgen examination. See detailed report below. Tumor removed surgically.*	Papilliferous, adenomatous islands are covered by high columnar epithelium. Stroma is of a myxomatous and mature connective tissue type, containing adipose cells and lymphoid tissue. Scattered throughout are islands of rudimentary bone formation. No cartilaginous element present. See detailed report below.

No.	Reference	Sex	Age	Gross Pathology	Microscopic Examination
50	Authors' Case No. 276643	M	24	*Tumor diagnosed from roentgenograms* which show an abnormal mass of great relative density surrounded by normal, air-containing lung. The tumor presents a sharply defined, lobulated border and contains within its outlines scattered irregular areas of even greater density, interpreted as calcium or bone. Diagnosis-primary pulmonary chondroma.	Tumor has not been removed. See detailed report below.

some structures within the neoplasm, although he could not demonstrate a connection with the normal bronchi. These bronchial areas are characterized by ciliated epithelium, the presence of a basal membrane, isolated lymphoid tissue, bundles of smooth muscle, and the presence of characteristic peribronchial tissue containing vessels, fat cells, and connective tissue. Our case No. 279994 resembles those of Bayer, although the location between the pulmonary lobes is rather distant for a tumor arising from a bronchial embryonal rest.

The analysis by Hickey and Simpson of the roentgenologic and pathologic findings in 40 cases gathered from the literature, including 2 cases of their own, is very complete. The first case of the series was reported in 1847. Roentgen examination was made in but 3, with identification of a tumor mass in 2. The remainder were discovered only at post mortem. Necropsy permitted

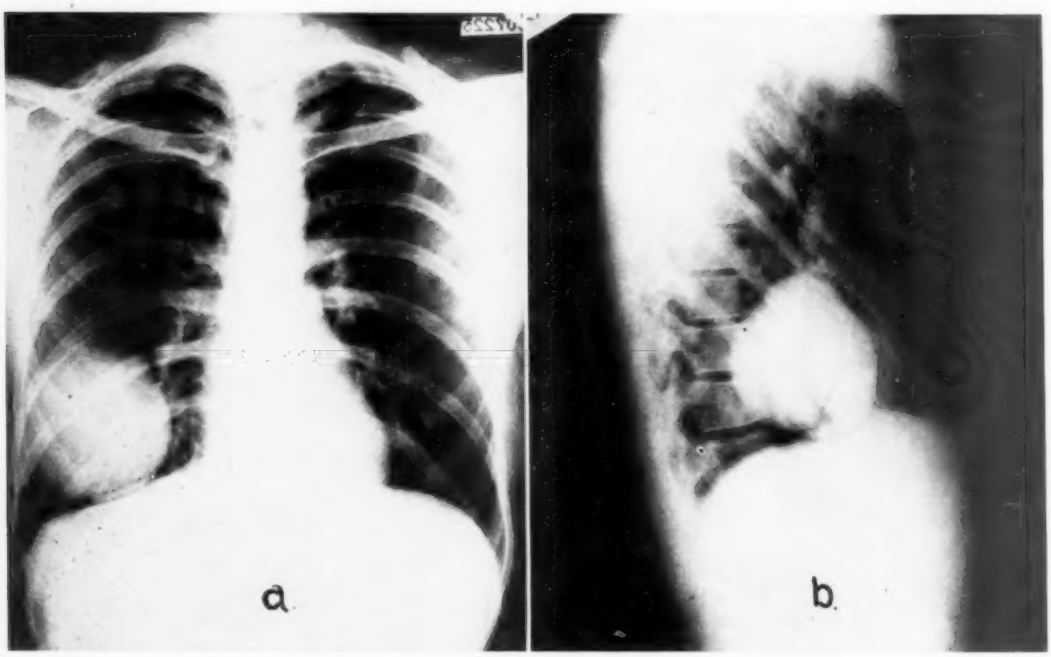

FIG. 1, *a* and *b*. Case 49. Tumor mass in right lower mid lung field, not attached to diaphragm; small irregular densities within tumor mass.

final classification also in those which had been seen ante mortem.

Since 1926 eight cases have been found in the literature. Again all but one were first discovered at necropsy. This one was reported by Klages, a German roentgenologist, in 1931. The tumor had been removed at operation, and two and a half years later the patient was reported as clinically well.

Detailed Report of Case 49. Farmer, aged thirty, Reg. No. 279994, was admitted to the University Hospital December 29, 1931, complaining of frequent headaches and an increasing ease of fatigue over a period of about one year. He remembered having had two or three night sweats in the spring of 1931. In March, 1931, the patient's teeth were repaired and five removed with no improvement. His tonsils were removed in June, 1931. Since June the patient had had discomfort in the pit of his stomach which was not relieved by food. He had slight nausea but no vomiting. Two weeks before entry the patient was awakened by a crushing sensation in the chest but does not recall on which side this occurred. He had lost 30 lb. in weight during the year.

At the time of admission to the University Hospital the patient had a subacute rhinitis with bilateral chronic maxillary sinusitis. The posterior right base of the chest was dull on percussion and breath sounds were diminished over this area. Blood Kahn reaction negative; blood and urine normal; complement fixation test for *Taenia ecchinococcus* was negative (made after tumor discovered in roentgeno- gram).

When referred to the Department of Roentgenology, the roentgenoscopic and film study of the gastrointestinal tract revealed no positive evidence of gross abnormality.

Stereoscopic studies of the thorax demonstrated a rather meager panniculus; normal bony cage; normal left diaphragm. Right diaphragm relatively normal, apparently somewhat pressed upon by a large soft tissue mass about the size of a large orange. This tumor was situated in the mid lung tissue slightly posterior to the usual position of the interlobar fissure. It extended from the under surface of the eighth rib to the upper surface of the eleventh posteriorly. The tumor was relatively homogeneous in density and it seemed to be in contact with the parietal pleura beneath the eighth and ninth ribs in the axilla (Fig. 1, *a* and *b*).

At that time the discussion of a differential diagnosis included a primary pulmonary chondroma, an ecchinococcus cyst, a pleural cyst, and as a remote possibility, a secondary neoplasm.

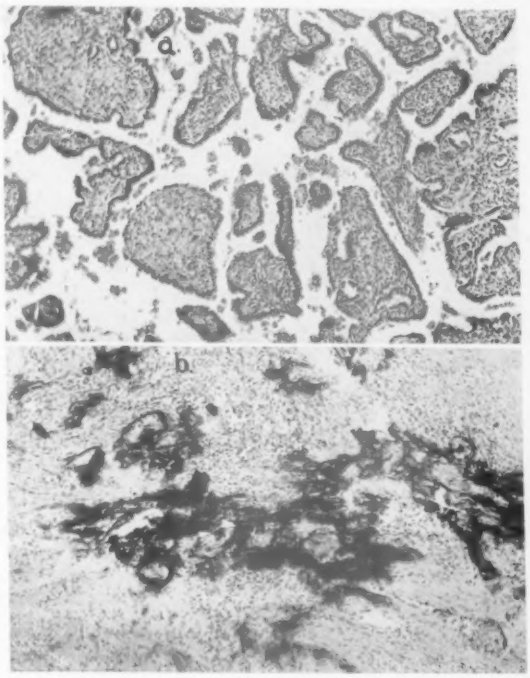

Fig. 2. Case 49. Photomicrograph. *a*. Papilliferous adenomatous islands—duct spaces lined by high columnar epitheiium; *b*, rudimentary bone fragments in loose connective tissue stroma.

In view of the recent admission of two patients with ecchinococcus cyst of the lung, the preoperative roentgen diagnosis favored this opinion, although primary chondroma was next in order of probability.

There was a possibility that some of the symptoms were of reflex vagus origin, and in view of the question of the tumor being an ecchinoccus cyst, the section on Thoracic Surgery thought it advisable to attempt to remove the mass.

At operation Dr. John Alexander, using local and regional anesthesia throughout, removed the right eighth and ninth ribs from the angle to the mid axillary line. No pleural adhesions were noted. The lung collapsed about 75 per cent. The right phrenic nerve was crushed to produce a temporary palsy of the right diaphragm. An encapsulated tumor was removed from its position adjacent to the interlobar fis-

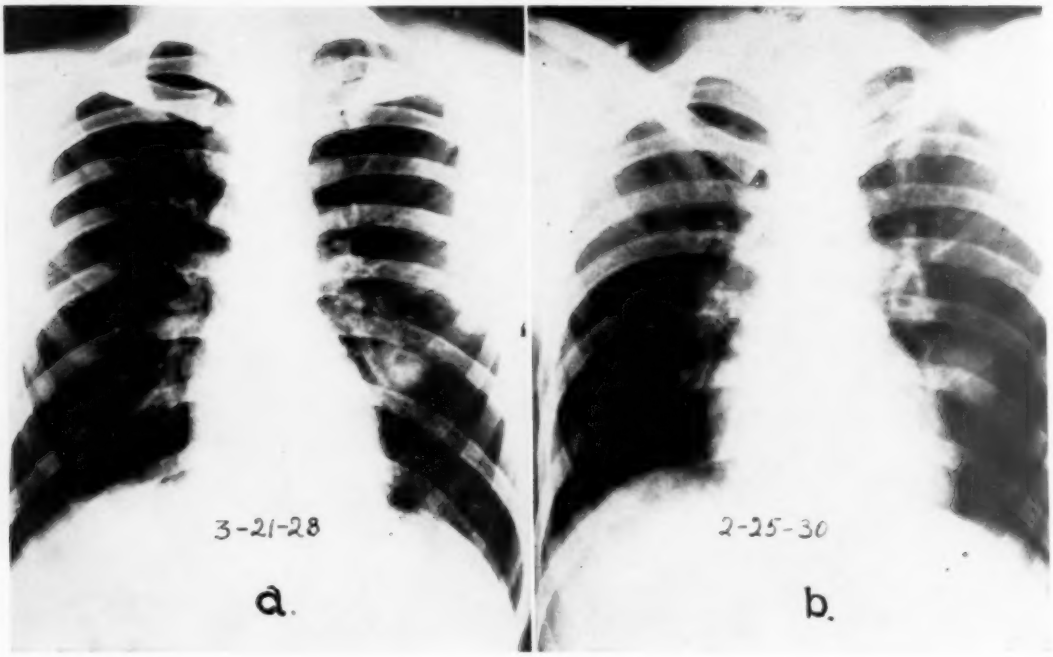

FIG. 3. Case 50. (Films loaned by Dr. J. B. Luckie of Pasadena.) *a.* March 21, 1928. A soft fairly homogeneous mass in left lung field near hilus. *b.* February 25, 1930. Roentgenogram taken with Potter-Bucky diaphragm. Mass definitely larger, lobulations and irregular increased densities in the mass are now seen.

sure without rupture of the capsule. Both lobes of the lung were densely adherent to the tumor capsule. The wound was closed and the patient returned to the ward in good condition.

Dr. Carl V. Weller described the specimen as follows:

3434-AJ *Gross Description:* The tissue is received in 10 per cent formol. It measures 6.1×6.1×5 cm. and weighs 200 grams. The mass is irregularly ovoid in shape and is encapsulated. It has a rubbery consistency and cuts with ease, but imparts a slightly gritty sensation to the knife. Cut surface shows a somewhat grayish color with many small bright yellow areas. Scattered through its substance are a few small spaces, the largest about twice the size of a cherry stone and surrounded by a myxomatous tissue. There are also occasional small lime salt deposits.

Microscopic Report: The tumor consists in large part of papilliferous, adenomatous islands covered by a high columnar epithelium, in some areas showing a pseudo-stratified arrangement. The stroma is made up of myxomatous and mature connective tissue showing some lymphocytic and plasma cell infiltration. In addition there are groups of adipose cells and islands of rudimentary bone formation. This is a variant in the group which more often shows extensive cartilage formation along with the mixture of tissue shown here. No malignancy, but well-marked cellularity indicates fairly rapid growth (Fig. 2).

Diagnosis: Papilliferous teratoid bronchial adenofibroma.

Following the operation the patient developed a hydropneumothorax. Thoracentesis was necessary several times during the first week with removal of considerable serosanguinous fluid (700 c.c.) at first, later decreasing progressively. The patient was discharged home on the twelfth day in good condition.

Two and one-half months after operation the patient was clinically well.

Roentgenoscopy then revealed normal excursion of the left diaphragm, complete fixation of the lateral portion of the right diaphragm with very little movement of the medial section. There was obliteration of the right costophrenic angle, no positive evidence of fluid.

Roentgenographic examination at this later time presented a normal appearance of the left bony cage and lung field. On the right side there was the surgical defect involving the eighth rib in the posterior axilla and the ninth rib in the mid axilla. The pleura was definitely thickened and fixed apparently in the axilla

along the sixth rib anteriorly and laterally, and the ninth posteriorly. There was a moderate amount of pneumonitis and residual pleuritis at the base.

Case 50. A male student, aged twenty-four, Reg. No. 276643, entered the Out-Patient Clinic complaining of recurrent asthmatic attacks since childhood. This was a familial characteristic as his grandfather and brothers and sisters have hay fever and asthma. The attacks occurred at irregular intervals, usually ushered in by a laryngitis and cough. Three days after onset of the upper respiratory infection asthmatic wheezing would occur. The attacks would last seven to ten days. Climatic changes seem to be of some benefit, as he had only three attacks over a period of six years when living in California, Arizona, and Florida.

He had moderate-sized, septic tonsils and an hyperesthetic rhinitis. The chest was normal in resonance, normal breath sounds, and no evidence of râles.

Blood, urine, and serology (Kahn) normal.

There was a marked allergic reaction by the scratch and intradermal methods, to poplar, short and long ragweed pollens; cabbage, orange, and rye; goose feathers; cat, dog, and horse dander.

Stereoscopic films of the chest Oct. 19, 1931, presented a normal bony cage, normal diaphragm, normal heart, moderate hilar infiltration on the right side, essentially clear parenchyma. On the left side there was a moderate perihilar infiltration. A nodular mass about 4 cm. in diameter appeared above the left lower main bronchus in a plane between the eighth interspace posteriorly and the fourth costochondral junction anteriorly. It was relatively homogeneous in density and apparently not connected with any specific hilar structure. Within this shadow were scattered irregular areas of even greater density interpreted as calcium or bone.

The singular character of the lesion tended to rule out both secondary neoplasm and tuberculous adenopathy. The relative freedom of the mediastinal glands eliminated in our opinion the possibility of a lymphoblastoma. The relative homogeneity would exclude a dermoid cyst, and the nodular character a simple cyst.

The roentgen diagnosis was one of the uncommon chondromata which are found in the lung (Fig. 4, *a* and *b*).

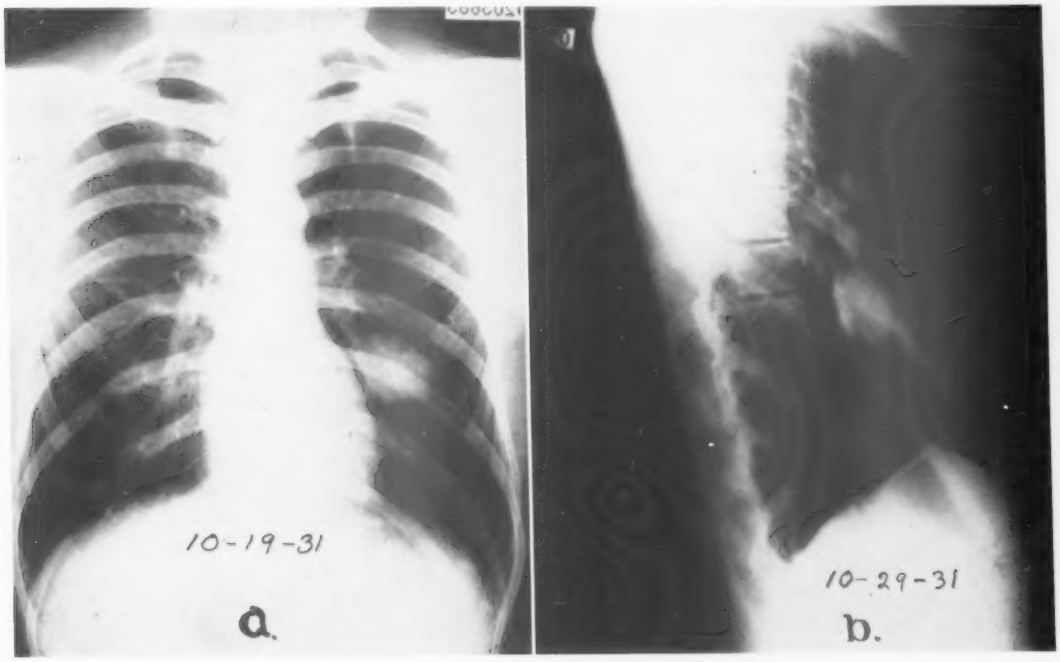

Fig. 4. Case 50. October 19, 1931. *a*. Discrete lobulated mass to the left and slightly below the hilus, containing areas of irregular, increased density. *b*. Lateral study showing position of mass in left mid lung field.

We then requested the privilege of review of the former films on the patient. We are indebted to the courtesy of Dr. James B. Luckie of Pasadena for these.

Roentgenograms of March 21, 1928, demonstrate a soft area of increased density, rather irregular, inferior and lateral to the left hilus (Fig. 3, *a*).

On April 17, 1928, this area was definitely circumscribed as of a mass distinctly separate from the hilus.

On May 10, 1928, it had taken on a lobulated character surrounded by normal lung, and had increased slightly in size.

A Potter-Bucky film made Feb. 25, 1930, again demonstrated an increase in the size of the tumor, the definite lobulated character was preserved and definite irregular greater densities had appeared within the tumor mass (Fig. 3, *b*).

This is then believed to be a progressively growing, essentially benign pulmonary tumor of the chondroma group. It is conceivable that some of the respiratory difficulty might be due to an exacerbation of a chronic infection of the lung in an area imperfectly aerated because of the presence of the mass, although there was at the time of examination no gross roentgen evidence of a marked inflammatory change. We were informed that his earlier visits to physicians at the time of the previous films were occasioned by a similar upper respiratory inflammation.

These cases resemble those previously reported both from the roentgen and microscopic appearance in that they present dense encapsulated masses with lobular contour, some irregularity in density as of calcareous fragments or bone. The microscopic section as well presents a multiplicity of tissue elements including cartilage, bone, papilliferous adenomatous islands, adipose tissue, lymphoid nests, and myxomatous connective tissue stroma.

CONCLUSIONS

Primary pulmonary chondroma is rare. However the occurrence must be greater than the meager literature suggests. With the increasing use of thorough roentgenographic examination of the chest more cases should be discovered.

The tumor is essentially non-malignant except when its location produces a mechanical obstruction.

It can be successfully removed by the surgeon, if necessary, when favorably situated, and without fear of recurrence.

The neoplasm is sufficiently characteristic roentgenographically to permit identification without microscopic study.

The courtesy of Doctor Gordon, in addition to those cited, is gratefully acknowledged.

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AN UNUSUAL CASE OF PLEURAL EFFUSION SIMULATING ELEVATION OF THE DIAPHRAGM*

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THE following case is reported because of the unusual form assumed by the pleural exudate. Even at necropsy a good explanation could not be ascertained. We have been unable to find reports of similar cases, and clinicians and roentgenologists of our acquaintance had never seen one.

CASE REPORT

The patient, a colored woman, aged nineteen, was admitted to Gallinger Municipal Hospital March 14, 1932, with complaints of nervousness, diarrhea and distention of the abdomen. One year before she had had an attack of diarrhea which lasted several weeks, cleared up spontaneously and was succeeded by a moderate degree of constipation. One month before she had noted that her abdomen was swelling and there was some indefinite abdominal pain and tenderness. This was soon followed by moderate diarrhea (3 to 4 movements a day) which lasted two weeks and then was checked by medication. During this time she was nauseated but did not vomit. The abdomen became more distended. The patient's usual nervousness increased markedly and became a prominent feature of her illness. There had been a loss of weight of 20 pounds in the past month. An infrequent, unproductive cough existed. The appetite had been good until two weeks before. Urinary symptoms were not present. Physical examination revealed a poorly nourished colored woman, who answered questions in a rambling, uncertain fashion. She was quite weak and complained of abdominal discomfort and tenderness, most marked in the region of the umbilicus and in the right lower quadrant. The abdomen was moderately distended and there was fairly good evidence of the presence of a moderate amount of fluid. Examination of the chest revealed decreased expansion at the left base with flatness

FIG. 1. Roentgenogram of chest with patient standing, showing fluid in left hemithorax simulating greatly elevated diaphragm.

FIG. 2. Roentgenogram of chest with patient supine, showing fluid spread out over left lung field and diaphragm in normal position.

* From the Medical Service of the Gallinger Municipal Hospital.

on percussion and absent vocal fremitus and breath sounds. Râles were not heard. The heart was definitely displaced to the right. The temperature was 101.2° F. The pulse rate was 120 per minute. The hemoglobin was 80 per cent

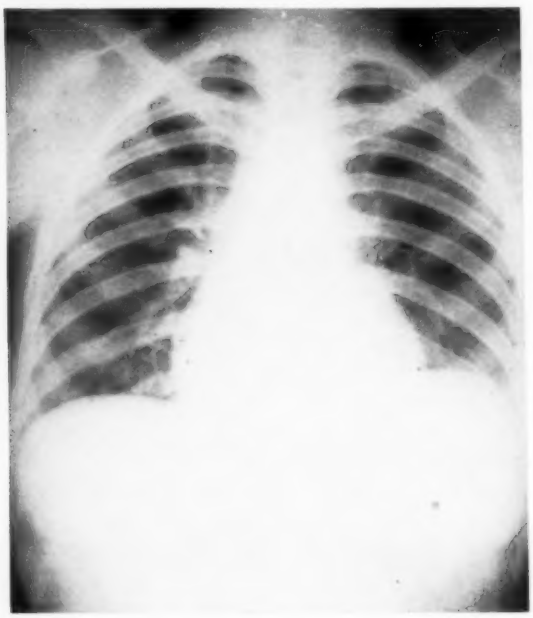

FIG. 3. Roentgenogram of chest with patient standing after withdrawal of 300 c.c. of fluid from left hemithorax. The false diaphragm is much lower than before aspiration.

(Newcomer); erythrocytes numbered 4,000,000 and leucocytes 9,000 per cubic millimeter of blood, with 61 per cent polymorphonuclears. Urinalysis was normal. The blood Wassermann was negative. Seven examinations of the sputum failed to show the presence of tubercle bacilli. A tentative diagnosis was made of tuberculous peritonitis with pleuritis and effusion in the left hemithorax. A roentgenogram of the chest showed what appeared to be a greatly elevated diaphragm on the left with some displacement of the heart to the right (Fig. 1). The patient was taken back to the roentgen department and the chest roentgenoscoped, first in the upright position. The apparently elevated left diaphragm moved up and down synchronously with the right, but at each beat of the heart a fluid wave passed across it. This fact led us to feel that there was fluid in the left hemithorax. In the recumbent position a startling change was noted. The whole left lung field became partially opaque as with fluid and a normally placed left diaphragm could be seen (Fig. 2). The patient was then slowly raised to the vertical position; there was no change in the picture until she was practically standing, when suddenly the original appearance returned. Lateral views did not help to explain the reason for this peculiar accumulation of fluid. The following day a needle was inserted in the eighth left intercostal space posteriorly and 300 c.c. of blood-tinged fluid was obtained. A subsequent roentgenogram showed the shadow of the false diaphragm to be much lower (Fig. 3). The left lung field was less opaque than before when the patient was recumbent. On April 20, two weeks later, re-examination showed a moderate increase in amount of fluid, and paracentesis in the same place as previously was productive of 500 c.c. of pale greenish fluid. The false diaphragm was again lowered. The patient ran a steady downhill course, with the temperature ranging from 101°F. to 104°F. and the pulse rate averaging 120 beats each minute. On April 28 she died. Necropsy revealed the peritoneum to be thickly studded with large, flat tubercles, and there was loculated fluid between coils of intestine. Tuberculous salpingitis was present. The thorax was carefully opened. About 500 c.c. of greenish fluid lay above the left diaphragm. There was a fibrinous pleuritis in the left hemithorax, but the fibrin was not thick, and the lung could be easily separated from the parietal pleura. The left lung was partially collapsed. A good explanation of the cause for the very unusual form which the pleural exudate assumed could not be derived from the necropsy. Apparently the fluid was encapsulated above the diaphragm by the fibrinous adhesions but escaped rather freely.

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STUDIES ON THE EFFECT OF ROENTGEN RAYS AND GAMMA RAYS UPON THE EGGS OF *DROSOPHILA MELANOGASTER*

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A. INTRODUCTION

IN order to compare the biologic effectiveness of measured quantities of roentgen rays and gamma rays of radium, we have used the eggs of *Drosophila melanogaster* for quantitative biologic tests because they have been found by previous workers[7] to be simple and satisfactory for this purpose. Furthermore, the quantities of radiation necessary to produce the desired effects are relatively small in comparison with those necessary for other methods of biologic assay, which usually require an amount several times that of the dosage used for therapeutic processes. The problem resolves itself into two parts: First, the production of an adequate number of satisfactory test objects, and second, the irradiation of the eggs with radiation intensities measured directly in r per minute for given radiation qualities. Since our technique for the production of the *Drosophila* eggs varies somewhat from that used by other workers, we wish to present in detail the arrangement we have found most satisfactory in our work.

B. *Drosophila* COLONIES

We have experimented for a considerable time with small colony jars commonly used for the flies but for various reasons, principally to obtain a sufficiently large number of eggs in a short period of time, we found it advisable to utilize museum specimen jars of 5 liter capacity for housing the flies (Fig. 1). This arrangement, furthermore, greatly simplified the handling of the flies. The jars were covered by glass plates held in place by a spring holder. The cover plate had two circular openings 2 inches in diameter to admit air, to permit transfer of the flies from one colony to another, and to offer a place to introduce microscopic slides (Fig. 1, *a*) covered with the egg-laying medium.

The medium used for feeding the flies is essentially the same as that used by Packard[7] and others. Fifteen grams of agar-agar are dissolved in 1,500 c.c. of water by heating the mixture. Then 100 c.c. each of baking molasses and blue-label Karo syrup are added. The heat is turned off and cornmeal is slowly stirred into the mixture until the consistency of the medium is such that it can be poured into the large jars; this quantity is sufficient for two jars. The medium is poured into the jars while they are upright and they are immediately tilted on one side so that the top of the jar is a few centimeters from the table, thus allowing the medium to cover one side of the jar.

When the medium has cooled and solidified any water that has condensed on the inside of the jar is wiped off, a suspension of baker's yeast in water is sprinkled over the surface of the medium and several paper towels are arranged in the jar to absorb liquid and also to furnish a dry surface upon which the flies can walk. The top of the jar is now put in place and some flies are introduced. Flies from an old colony can be transferred to a fresh jar through a glass tube that is sufficiently large so that with a heavy rubber band over the end it just fits into the hole in the lid of the jar. The jar to be emptied is covered with a cloth to darken it and the flies, being positively phototrophic, are attracted over into the fresh jar.

A banana-agar gel was used in collecting eggs for irradiation. This is prepared in the following way: Six bananas are mashed through a potato ricer and 600 c.c. of water

added in order to dissolve out organic substances. The mixture is heated slightly and filtered while hot through a cloth towel. The filtrate should not be allowed to cool

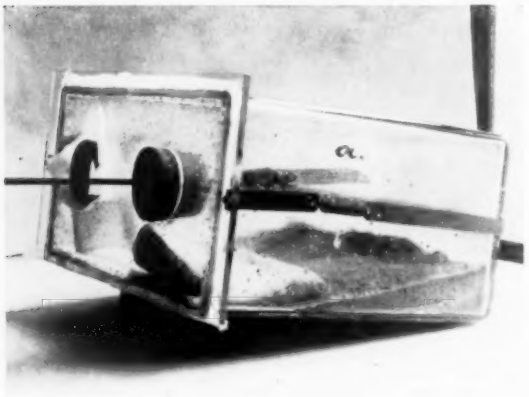

FIG. 1. Colony jar for *Drosophila*. *a*—Microscope slide covered with egg-laying medium.

before it is added to the second solution because on cooling it forms a gel which does not liquefy again readily. A liter of 2 per cent agar solution is prepared and filtered while hot through a cloth towel and this filtrate is added to the banana filtrate. This banana-agar mixture can now be poured into a number of Petri dishes to a depth of approximately 4 mm. and allowed to cool. The Petri dishes and any excess of banana-agar can be stored in a refrigerator until needed. There is no need for sterilizing the medium unless the refrigerator temperature is insufficient to prevent the growth of microorganisms.

To use the banana-agar, rectangular strips about 25 × 50 mm. are cut from the medium in the Petri dishes and placed upon microscope slides and put into the colony jars for an hour or two. If a membrane has not formed over the surface of the agar due to dehydration the flies will lay most of their eggs on the top of the agar. Otherwise they are likely to lay most of them on the cut edges, which makes it difficult to count them. Normally a small percentage of the eggs are deposited on the cut edges of the banana-agar and if one wishes these can be scraped off with the point of a probe and placed on the top of the strip.

Several factors have been observed which must be controlled in order to keep the colonies in good condition. Doubtless there are numerous other less significant factors which enter into the problem but we have observed essentially the following:

1. *Temperature:* If the colonies are kept at too high a temperature, the fermentation takes place too rapidly and the flies will lay eggs only for a few days; 23°C. has been found to be a satisfactory temperature. The flies might do better at a higher temperature if it were not for the rapid changes which occur in their food at these temperatures.

2. *Humidity:* Since the air surrounding the colonies is almost continuously saturated with water vapor, the inside of the colony jar becomes quite damp as time goes on and this is undesirable. The occasional introduction of a dry paper towel will aid in prolonging the egg-producing period of the colony.

3. *Bacterial activity:* If other organisms than the yeast assume an early domination of the colony few eggs will be produced. This is the reason for starting the colonies as soon as the jars are prepared unless one

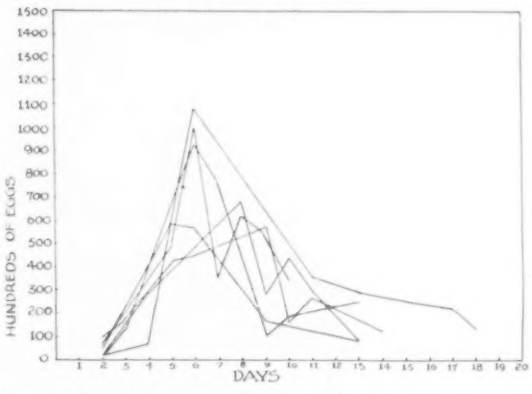

FIG. 2. Graph showing number of eggs per day from different colonies.

wishes to have the jars sterile and keep them so until used.

4. *Parasites:* Mites have been reported by geneticists and others working with

Drosophila melanogaster and we have encountered them on several occasions. Once introduced into a colony they soon ruin the colony and apparently the only way to get rid of them is to discard the flies and start over again with a few flies that are free from parasites. For this reason stray flies should not be allowed to get into the colonies at any time.

5. *Light:* Colonies were kept for three months in a room in which the only source of light was an incandescent bulb which was lighted for a few hours each day, and under these conditions the quality of the eggs apparently was not affected as a result of the quality or intensity of radiation to which they were subjected.

Once a colony is started it follows a fairly definite cycle. The first few days very few eggs are laid but about the fourth or sixth day the egg production rises to a maximum and gradually decreases after this time. With decreasing egg production the quality of the eggs may or may not vary. It is important to check the natural death rate of the eggs continuously in order to ascertain whether they are satisfactory for radiation tests. The change in the number of eggs laid per day is illustrated for a number of the colonies in Figure 2. Table 1 shows the figures for one single colony.

TABLE I

DATA FOR EGG PRODUCTION CURVE

		Colony No. 7.	
Days	Eggs	Days	Eggs
1	0	10	(not counted)
2	12	11	357
3	14	12	254
4	66	13	290
5	50	14	156
6	1079	15	223
7	(not counted)	16	(not counted)
8	(not counted)	17	217
9	(not counted)	18	135
			Total 3,566

NOTE: During the period when eggs were being collected from a colony the light was excluded by covering the jar with a dark cloth. This was merely to prevent outside disturbances from exciting the flies. If there are no disturbances in the room the flies will lay equally well in the light or in the dark.

If the eggs from four colonies are collected for an hour or two each day the number obtained should average 1,000 per day and some days will amount to several times this figure. After a colony no longer produces a sufficient number of eggs, the flies

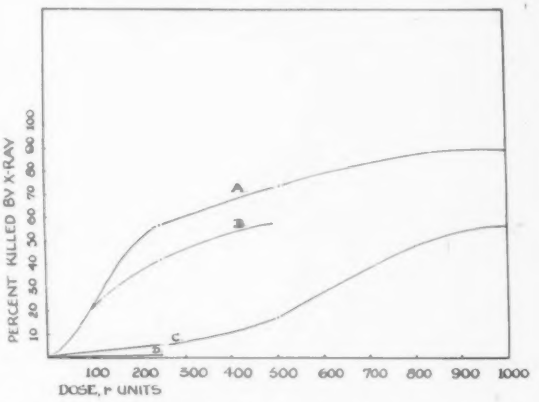

FIG. 3. Graph showing variation of radiosensitivity of *Drosophila* eggs in relation to time after laying.

in it should be transferred to a new colony jar. The flies from two old colonies can be put into one fresh jar. The old jars are then set aside for ten days or two weeks while the recently laid eggs and larvae have an opportunity to develop into flies; then the flies from the two colonies can be transferred to a fresh colony jar. Twelve jars are sufficient to keep four colonies producing eggs continuously.

C. FACTORS INFLUENCING RADIOSENSITIVITY OF *Drosophila* EGGS

If the eggs which are laid within a short period of time (for instance, one hour) are examined it will be noted that a few of them already will be hatched and if examined an hour or two later it will be noted that more have hatched in the meantime. In other words, a group of eggs just laid is very heterogeneous as regards the degree of individual development. If there is a variation of radiosensitivity with the developmental age of the individuals then unless we have groups of eggs with a similar distribution of developmental ages this may be a serious source of error in making any absolute

measurements of radiosensitivity with this method.

D. TECHNIQUE OF CONTROLLING EGGS FOR IRRADIATION

The eggs were counted immediately after irradiation and both the number of unhatched eggs and the number of hatched eggs were recorded. The latter number is a rough measure of the degree of development of the eggs as a group. The eggs were then set aside for a period of forty hours at a temperature of 25°C., forty hours being ample time for all the eggs to hatch that were not killed, after which time the remaining unhatched eggs were counted. The unhatched eggs can be distinguished quite easily at the end of forty hours while it would be difficult at the same time to make an accurate count of the empty shells. A binocular dissecting miscroscope was found to be very convenient for making the count, and a counter for recording two different kinds of cells was found to be quite indispensable.

In the early work of attempting to correlate the physical dosage in roentgens with the lethal effect on the eggs, considerable variation was observed in the effects of a given quality and quantity of roentgen rays. An effort was made to determine the cause of this variation and, so far as possible, to determine the factors involved.

The relationship between the radiosensitivity and age was investigated first. Eggs were collected from three colonies over a period of four days. The eggs from 8:00 A.M. to 10:00 A.M. were set aside at room temperature (30°C.) and irradiated at 1:00 P.M. with the eggs laid from 10:00

TABLE II

Colony	Control			8:00 A.M. to 10:00 A.M. Irradiated with 250 r, 90 kv. 1 mm. Al, 2 min., 15 sec. at 33.3 cm.			10:00 A.M. to 12:00 noon Irradiated same as 8:00 A.M. to 10:00 A.M.		
	Total eggs hatched	Eggs not hatched	Percentage of eggs not hatched	Total eggs hatched	Eggs not hatched	Percentage of eggs not hatched	Total eggs hatched	Eggs not hatched	Percentage of eggs not hatched
4	257	9	3.5	491	18	3.7	172	77	44.0
5	599	20	3.3	1,068	53	5.0	330	146	45.0
6	269	11	3.7	624	31	5.0	727	334	46.0

TABLE III

EXPERIMENT SIMILAR TO THAT IN TABLE II AT A HIGHER DOSAGE (620 r)

Colony	12:00 noon to 1:30 P.M. Irradiated at 1:45 P.M.			10:00 A.M. to 12:30 P.M. Irradiated at 1:15 P.M.		
	Total eggs hatched	Eggs not hatched	Percentage of eggs not hatched	Total eggs hatched	Eggs not hatched	Percentage of eggs not hatched
7	131	119	91	57	30	53
8	140	125	89	217	166	76
10	42	39	93	153	107	71
	Total 313	Total 283	Average 90	Total 427	Total 303	Average 66.6

A.M. to 12:00 noon (Tables II and III).

These results indicate that there is a great change in radiosensitivity with developmental age. Since the developmental age is a function of the temperature and time, we have used time as an expression for age and have carried out the work during a period of time when the temperature was fairly constant.

In attempting to work out more completely the variation of radiosensitivity in relation to time after laying, different ages of eggs were exposed to various doses of a radiation produced with 90 kv., 4 ma. and filtered through 1 mm. of aluminum (effective wave length 0.66 Å). The results are illustrated in Table IV and in Figure 3. Of course this relationship is also a function of the temperature since there is no sufficiently precise way to determine the developmental age of the eggs. One must rely upon the relative ages as expressed by time, keeping the temperature constant. The death curves for various other dosages of roentgen rays when studied in relation to the developmental stages of the eggs were worked out in more detail with the results collected in Table V and graphically represented in Figure 4.

If we define radioresistance as "100 minus per cent killed" then for 250 r there is the relation shown in Table V.

These results* indicate that if *Drosophila*

TABLE IV

Dose	Total eggs hatched	Controls: Eggs not hatched	Controls: Percentage of eggs not hatched	Irradiated: Total eggs hatched	Irradiated: Eggs not hatched	Irradiated: Percentage of eggs not hatched	Irradiated: Percentage of eggs killed
A. Laid in one and one-half hours. Irradiated one-half hour later.*							
250 r	477	32	6.7	1,091	693	63.5	56.8†
500 r	71	3	4.2	162	125	77.2	73.0
750 r	415	23	5.5	933	786	84.2	78.7
1,000 r	308	14	4.5	666	628	94.3	89.8
B. Laid in two hours. Irradiated one hour later.*							
125 r	145	9	5.5	405	128	31.6	26.1
250 r	1,125	40	3.5	1,229	557	45.3	41.8
500 r	—	—	5.0	1,452	898	61.8	56.8
C. Laid in one and one-half hours. Irradiated two hours later.*							
250 r	348	10	2.9	581	49	8.4	5.5
500 r	262	8	3.0	420	84	20.0	17.0
1,000 r	129	4	3.1	251	146	58.2	55.1
D. Laid in two hours. Irradiated four hours later.*							
250 r	1,125	40	3.6	2,183	102	4.6	1.0

* Colonies were kept at a temperature ranging from 22°C. to 24°C. Immediately after being laid the eggs were taken to temperature of approximately 30°C.

† Equals number dead minus the control death rate.

* During the course of the work several strains of wild *Drosophila* were used and the results from each strain were consistent with the present work. No special study was carried out to ascertain whether there is an appreciable variation in radiosensitivity in different strains. The present work was done with a reverted full eye from a bar eye type (Zeleny, #2054.1). The only morphologic difference between this strain and the wild type is forked

eggs are to be used as a measure of roentgen-ray or gamma-ray dosage the end-result will be decidedly influenced by the developmental stages represented in the test eggs. Since we have no accurate way to

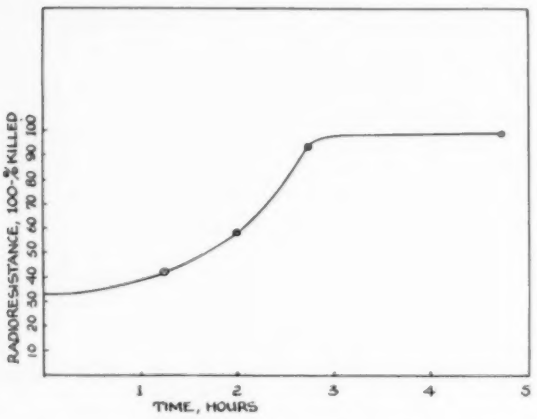

Fig. 4. Graph showing death curves of *Drosophila* eggs for various dosages of roentgen rays in relation to the developmental stages of the eggs.

evaluate the developmental factor for a heterogeneous group of eggs, their utilization in absolute measurements of dosage are of little value. However, this does not destroy the usefulness of the eggs for comparative studies of the effects of different irradiations. We can easily obtain two similar groups of eggs by dividing the eggs produced by a given colony during a given period of time into two portions. According to the probable distribution of the eggs on the agar strips it can safely be assumed that there are two biologically equivalent groups of eggs if the whole quantity is divided into two portions, providing, of course, that a sufficient number of trials is made to minimize the probable error. In this way we can say that two given quantities of radiation are equivalent in a biologic sense when they produce an equal injury on similar groups of eggs.

bristles. Genetically there are some differences between this strain and wild strains. The strain used was obtained from Dr. A. H. Hersh of the Department of Biology, Adelbert College, Western Reserve University, Cleveland, Ohio, to whom we wish to express our appreciation for his kind help.

D. PHYSICAL MEASUREMENTS

Drosophila eggs were irradiated with measured doses of both roentgen rays and gamma rays of radium. Our method and the apparatus used for the experimental definition of the International Unit of roentgen radiation, r, for roentgen rays has been described previously.[4] We used the large air ionization chamber which, together with the whole measuring arrangement is illustrated in a diagram in Figure 5. We wish to present again a few of the more important features of this arrangement.

The collector plate (E_1) of the large air ionization chamber has a surface of 4.983 $\times$ 20 cm. each. E_2, E_2 are guard plates. The connections of these plates are insulated with amber and bakelite. The electrode (E_3), which is opposite these plates, has a surface of 26.98 $\times$ 20 cm. The distance between E_1 and E_3 is 10 cm. Measurements with varying distances for the hardest rays used in our experiments showed that this distance is sufficient to include all the ions which are created by the radiation which enters the chamber. The chamber is constructed in such a way that the roentgen beam will pass through it vertically. Only those ions which are formed in the air volume in the frustum of a cone with the

Table V

	Time*	Radio-resistance
Laid in 1 hr. 30 min. Irradiated 30 min. later	1 hr. 15 min.	42
Laid in 2 hr. Irradiated 1 hr. later	2 hr.	58
Laid in 1 hr. 30 min. Irradiated 2 hr. later	2 hr. 45 min.	94
Laid in 1 hr. 30 min. Irradiated 4 hr. later	4 hr. 45 min.	99

* Time from middle of laying period to time of irradiation

height equal to the width of the electrode E_1 and the diameter equivalent to the opening diaphragm of the ionization chamber are measured. The diameter of the lead diaphragm (D_3) is 8 mm. and it has a thickness of 4 mm. The effective length of E_1 is 5.02 c.c. The diaphragm (D_3) is mounted on a lead pipe 10 cm. in length. A similar pipe

is used at the opposite end where the roentgen beam leaves the ionization chamber. This pipe carries a mirror Sp which permits accurate sighting of the focal spot through the whole apparatus. The system of diaphragms (D_1, D_2, D_3, D_4, and D_5) was carefully selected in order to permit all the radiation from the focal spot (which had a diameter of about 8 mm.), and from this focal spot only, to enter the chamber. Pin hole pictures and special tests described previously proved that our diaphragm system was sufficient to shield the ionization chamber from all undesired radiation.

The collector plate E_1 of the air chamber is connected to a gold leaf electroscope (M) by means of a connection (Z) 125 cm. in length. The insulation within this connection is of amber and ceresin which insulates the system perfectly. The chamber and the electroscope system are completely enclosed in grounded metal tubes and housings.

The sensitivity of the apparatus was controlled by means of a special battery (B_1) which could be added to the total battery (B_2) which was used to charge the electroscope. This special battery of 23.5 volts was so arranged that by adding it the filament of the electroscope went over the same five divisions which were used when making measurements of the ionization current. Plate E_3 is charged to a potential of 1,500 volts which is furnished by a direct current generator (H). The tension of the battery (B_2 and B_3) and that of the direct current generator were measured by technical voltmeters and that of the battery B_1 by means of a Weston precision voltmeter.

The capacity of the whole system was determined by means of a Seibt capacity bridge which was calibrated at the Bureau of Standards. Under given radiation conditions, the intensity per minute which is effective at the site of the diaphragm B_3 in roentgens, is calculated by the well-known formula $\frac{C\times(V_2-V_1)\times 60}{300\times vol.\times t}$ r/min. where C is the capacity of the whole measuring system in centimeters, (V_2-V_1) is volt sensitivity in volts, *vol.* is the effective air volume in cubic centimeters and t is the time in seconds of discharge of the electroscope over five divisions.

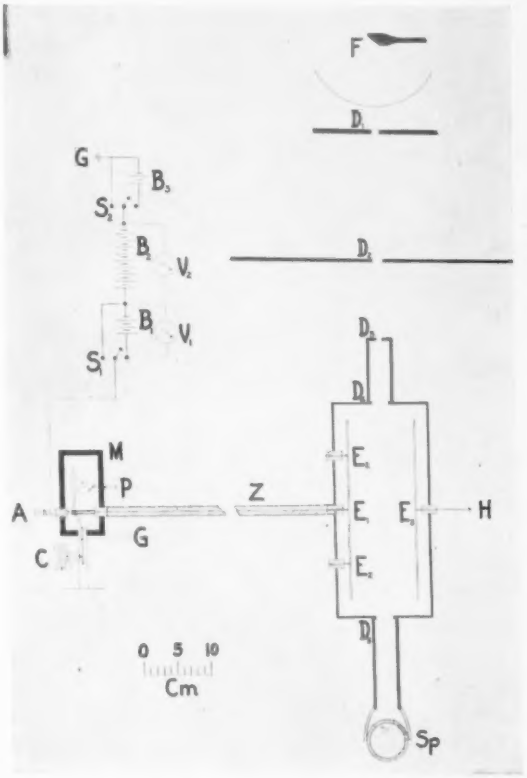

Fig. 5. Standard air ionization chamber.

The roentgen-ray intensities used in our experiments presented in this article were determined with this large air ionization chamber system. We may add that comparisons between the roentgen determined in our laboratory and that in other calibration institutions has shown them to be in very satisfactory agreement.

Another procedure for the finding of the standard roentgen was first presented by Fricke and Glasser in 1925, and was described in detail at that time.[1,2] By this method, instead of the large air ionization chamber a small ionization chamber with a volume of 1 c.c., the walls of which have an effective atomic number equal to that of atmospheric air, was used. We have

demonstrated that under certain conditions such a chamber will register the dose directly in roentgens when the electrical constants, volt sensitivity, and capacity of the measuring apparatus are once established.

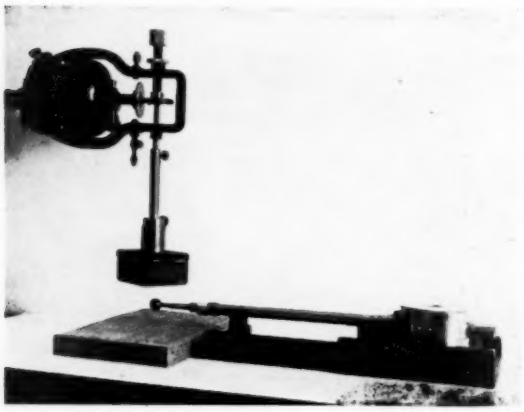

FIG. 6. Determination of intensity of gamma rays of radium pack with condenser dosimeter.

We use such small ionization chambers to measure the intensities of gamma rays of radium in our experiments. We are well aware of the fact that this is an indirect method of determining the radiation intensities of radium and that the method itself may not yet rest on sufficiently well-established theoretic foundations; however, we present our method in the manner used in our experiments and believe that if further research work should disclose new features which have not been taken into consideration in our measurements, suitable corrections may easily be made. We used the condenser dosimeter which also has been described.[4,5,6] It consists of two parts: first, a condenser to which an ionization chamber is attached, and second, an improved type of string electrometer including a static charger. For dosage measurements the apparatus is used in the following manner: The condenser unit is connected electrically with an electrometer unit and the whole system is charged to a known potential which is indicated on the electrometer scale. The condenser unit is then removed and placed with its ionization chamber in the field of radiation to be measured. After being exposed for a specified time, the condenser unit is again returned to the electrometer and the loss of charge is read directly on the scale. If the material and size of the ionization chamber have been properly selected and if the electrical capacity and volt sensitivity of the instrument are known, the loss of charge indicated on the scale can be directly converted into roentgens. In order to prevent any radiation from affecting the charge in the condenser unit other than at the ionization chamber, a solid dielectric completely surrounds the charged part of the system. In this way the use of lead is dispensed with. The formula by which the radiation intensity in roentgens is obtained from the measurements and constants of the condenser dosimeter is similar to the formula mentioned above.

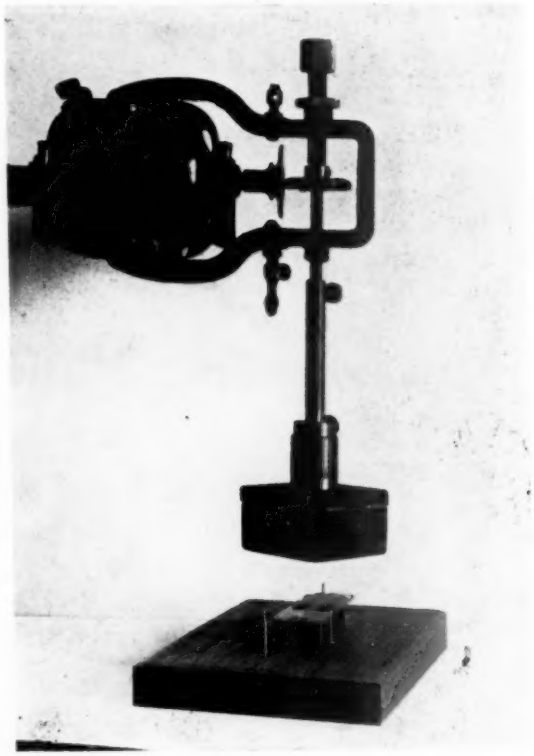

FIG. 7. Irradiation of *Drosophila* eggs with rotating radium pack.

The capacity of our complete system is 80.0 cm. In most of our measurements a volt sensitivity of 4.5 volts per division was selected. For the determination of the intensities of gamma rays of radium we used natural leakage of the instrument was extremely small and could be disregarded. The set-up used is illustrated in Figures 6 and 7. The distance between the radium preparation which could be rotated con-

TABLE VI

DISTANCE OF RADIUM PACK TO EGGS APPROXIMATELY 3 CM.; ROENTGEN RAYS 140 KV., 2 AL, AT DISTANCE TO GIVE SAME EXPOSURE TIME AS RADIUM—APPROXIMATELY 1 METER.

Treated with Radium			Treated with Roentgen Rays	
Date of treatment	Percentage of of eggs hatched	Dose of radium used	Percentage of eggs hatched	Dose of x-rays used
June 4, 1930	57.4 66.4	450 r	67.8 55.2	300 r
June 3, 1930	63.2 52.0	450 r	58.4 51.7	300 r
June 2, 1930	66.6 58.7	450 r	63.4 61.5	300 r
June 1, 1930	65.4 47.0 ?	450 r	59.2 56.2	300 r
May 27, 1930			57.2 59.2	300 r
May 26, 1930	53.7 36.1 ?	450 r	44.7 60.5	300 r
May 24, 1930	63.7 69.3	450 r	53.5 79.5	300 r
May 22, 1930	55.8 56.1	450 r	81.5 78.2	225 r
May 20, 1930	53.0 64.0	450 r	30.0 49.4	275 r
May 18, 1930	49.0 50.2	450 r	70.0 57.0	275 r

mostly the small air wall ionization chamber of a volume of 1/35 c.c. In making these measurements special precautions had to be taken to avoid natural leakage of the instrument or the effects of undesired radiation upon the dielectric. The latter effect was continuously checked by replacing the ionization chamber by an amber clad metal cap and then exposing the condenser unit to the radiation. The tinuously and the biologic specimen or the ionization chamber could be accurately determined on a scale with a Vernier arrangement.

E. COMPARISONS BETWEEN ROENTGEN RAYS AND RADIUM RAYS

A large series of experiments was made in order to determine the relative effectiveness of roentgen rays of various wave-

lengths and also of roentgen rays and of gamma rays. Efforts were made to determine accurately the death curves for various qualities of roentgen rays but due to the difficulties with the eggs no final results have as yet been obtained. Of special interest was the study of the comparative effectiveness of roentgen rays and gamma rays. These comparisons were carried out in the following manner, taking the necessary precautions to avoid the sources of error already discussed: The colonies were kept at a constant temperature and the eggs collected during a period of two hours at a given time of day and irradiated immediately afterwards. The doses of roentgen rays and radium were measured as described in the discussion of the physical apparatus. All the roentgen rays used in these special experiments were produced by 90 kv., 4 ma., 2 mm. Al filtration, and had an effective wave-length of 0.66 Å. The radium radiation was obtained from a pack such as was described previously[3] (4 × 4 cm area, and 4 mm. brass filter). To avoid errors due to differences in the duration of the exposure in the two cases the same roentgen intensity was always used as obtained from the radium pack making an equal exposure time to each of the radiations. The order of the intensity in most of the experiments was about 10 r per minute. Efforts were made to avoid back-scattering by placing the medium covered with the eggs on gauze strips stretched across the field of radiation when roentgen rays were used. In the case of gamma rays the medium and eggs were placed on glass slides. Special measurements were made with the ionization chamber on a solid medium and no appreciable back-scattering was found. The counting of the eggs and the evaluation of the results were carried out as described in the preceding discussion of the biologic problem. The results of a series of experiments are collected in Table VI.

The results show that the average percentage of eggs killed by 300 r of roentgen rays was 42.9 per cent. The average for 450 r of gamma rays was 40.9 per cent. These qualities represent equal biologic effectiveness making 450 r of gamma rays as measured with our condenser dosimeter method equivalent to 300 r of roentgen rays of the stated quality. This difference in biologic effectiveness between roentgen rays and gamma rays of radium is similar to, but not as pronounced as, that upon the human skin reported by us previously.[5]

In conclusion, we wish to express our appreciation of the assistance offered by Mr. I. E. Beasley in the experimental part of this work and in the construction of the apparatus used.

SUMMARY AND CONCLUSIONS

1. A technique for production of large numbers of eggs of *Drosophila melanogaster* which can be satisfactorily used as radiation test objects is described.

2. The various factors which influence the natural mortality rate of the *Drosophila* eggs are investigated.

3. *Drosophila* eggs in various stages of development were irradiated with measured doses of roentgen rays and gamma rays of radium and their mortality rate was subsequently observed.

4. Owing to numerous factors which influence this mortality rate outside of the effects of radiation, the *Drosophila* eggs do not appear to be suitable for absolute determinations of radiation doses.

5. If the quality of the eggs is properly controlled simultaneous comparisons between the effectiveness of roentgen rays and gamma rays of radium can be made.

6. Such comparisons were made and it was found that a dose of 300 r of roentgen rays in its effect upon the death rate was equivalent to 450 r of gamma rays of radium.

7. This difference in biologic effectiveness between roentgen rays and gamma rays of radium is similar to, though apparently not as pronounced as, that observed upon the human skin.

8. A description of the technique of the physical dosage measurements is given.

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THE COMPARISON OF HIGH VOLTAGE ROENTGEN-RAY GENERATORS*

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Bureau of Standards, Washington, D. C.

ABSTRACT

It is shown that when measurements are made in the customary manner, the roentgen-ray emission of a tube operated on two mechanical rectifiers may differ by ±20 per cent, although the electrical indications are the same. This also applies to quality evaluations whether of the full absorptive curve, half-value layer or effective wave length type.

Determinations of percentage depth dose do not show any such marked differences since this is a comparatively insensitive indicator. It is seen, moreover, that there is little gain in percentage depth dose in going from 160 to 200 kv. peak, the only change of significance being in the actual 10 cm. depth dose.

It is shown, on the other hand, when the potential of three generators, including constant potential, is measured in effective kilovolts that for a given potential, the roentgen-ray outputs for a given filtration and given current are all very nearly the same, both as regards intensity and quality.

I. INTRODUCTION

IN THE technical and clinical use of high voltage roentgen rays, a wide variety of generators has come into common use. To save strain on the roentgen tube, unidirectional voltage, obtained by mechanical or by thermionic rectifiers, is usually applied. Since the rectification characteristics of such generators differ widely, there has been considerable confusion as to their relative effectiveness in producing the desired therapeutic or technical results.

Experience in this laboratory has led us to the conclusion that, due largely to the

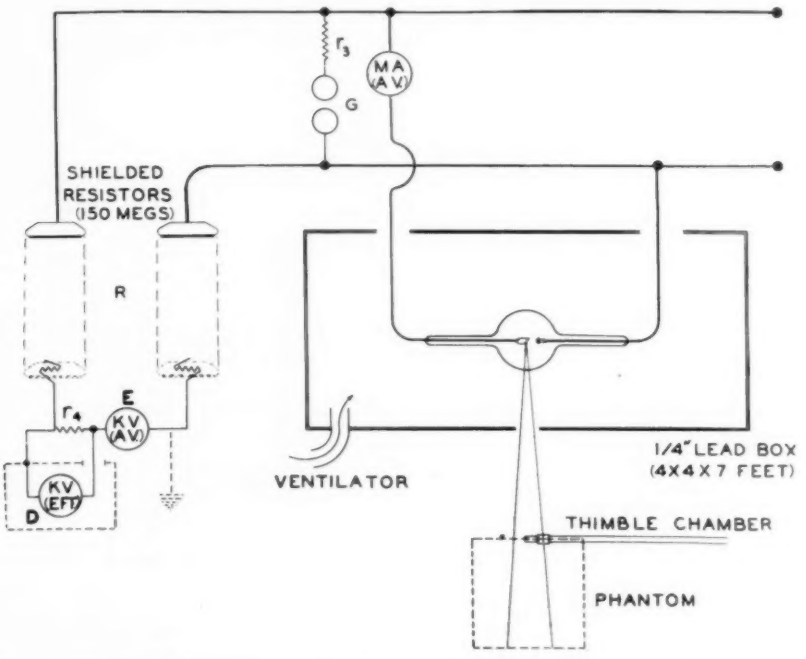


FIG. 1. Diagram of apparatus showing current and voltage measuring systems.

* First part of paper presented at joint meeting of the American Association for Advancement of Science and the American Roentgen Ray Society, Syracuse, N. Y., June, 1932.

† Research Associate, Radiological Research Institute. This work was started by K. L. Tucker who by reason of illness was obliged to withdraw from active participation before the experimental work was complete.

lack of properly controlled experimental conditions, comparisons between roentgen-ray generators which have been made in the past are of questionable soundness. For example, we have found that a different roentgen-ray emission, as expressed in terms of the ionization produced in air, is

The physical equality of roentgen beams produced by different generators, so far as concerns therapeutic application, has been shown to be based on 10 or more factors.[1] Included in these are tube current, tube voltage (peak), filter, quality (half-valve layer or λ_e),[2] roentgens per minute

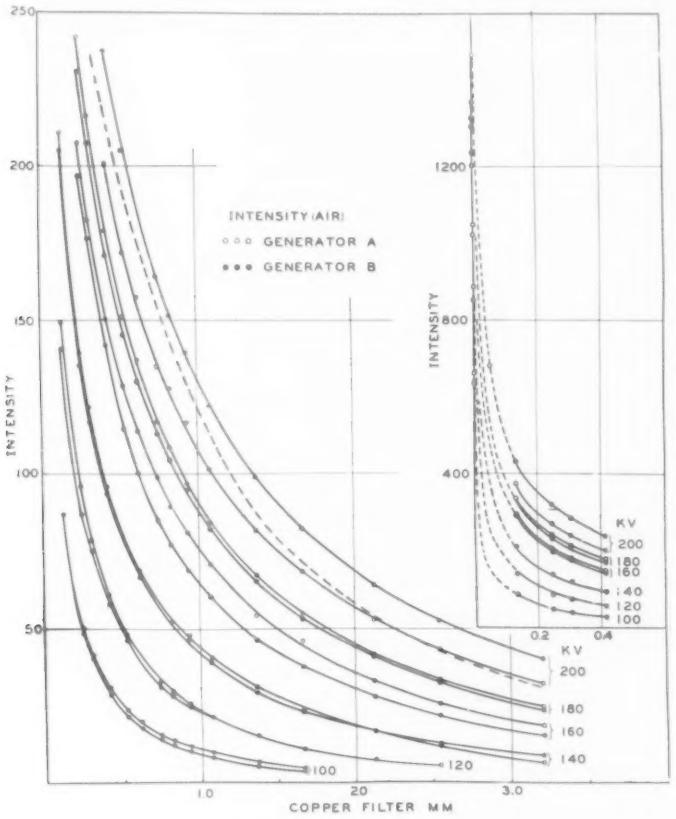


FIG. 2. Beam intensities for generators *A* and *B* measured in air. Broken curve is for 150 kv. (av.) on generator *C*, taken from Figure 3.

obtained from a given tube and generator when either the aerial system or the tube enclosure is changed.

It was decided, therefore, to make a careful comparison of several typical roentgen-ray generators having as few variables as possible and yet under as nearly clinical operating conditions as obtainable in a laboratory. For the most part, the various quantities were measured in the same units and in the same manner as in the clinic so that the results may be readily interpreted in commonly used terms.

delivered by tube,[3] and percentage depth dose.[4]

[1] Pohle, E. A. Dosimetry in roentgenotherapy. AM. J. ROENTGENOL. & RAD. THERAPY, 1927, *18*, 55–56.

[2] The half-value layer (H-V.L.) in copper or aluminum is a measure of the "penetrating power" of a roentgen beam. It is defined as the thickness of copper (or aluminum) which interposed in a roentgen beam reduces its intensity to one-half its initial value (as measured in terms of air ionization).

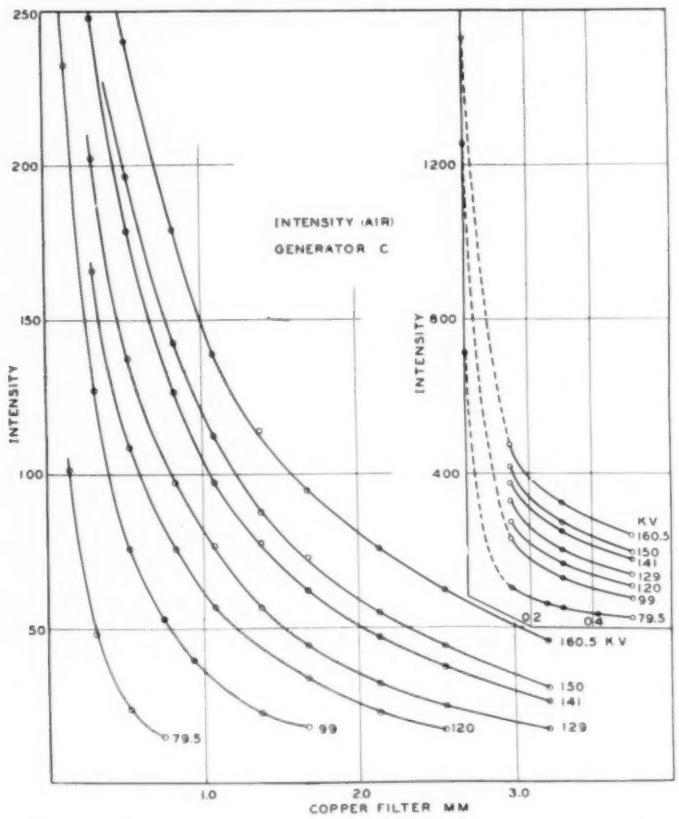
The effective wave length of a roentgen beam is the wave length of the homogeneous radiation having the same absorption coefficient in copper (or aluminum) as the heterogeneous radiation in question. (See discussion of various methods of expressing roentgen-ray qualities in a paper by L. S. Taylor, *Bur. Standards J. Research*, 1930, *5*, 517 (RP 212).

[3] The "roentgen" (r) is defined as the quantity of radiation which, when the secondary electrons are fully utilized and the wall effect of the chamber is avoided, produces in one cubic centimeter

II. APPARATUS

Three generators, *A*, *B*, and *C*, were chosen as typical. *A* and *B* were rated to deliver full wave 220–230 kv. (peak) at 30 milliamperes. *C* was rated to deliver 200 kv. (peak) at 10 milliamperes. *A* was a mechanical rectifier having a single high-ripplage[5] of only about 1.5–2 per cent per milliampere, and hence a roentgen-ray emission not differing appreciably from strictly constant potential.

Any one of the three generators could be alternately connected to the same overhead system without changing its capaci-



[Fig. 3. Beam intensities for generator *C* measured in air.

tension transformer and rectifying approximately 30 degrees of the cycle. *B* was a mechanical rectifier having a divided secondary high-tension transformer and rectifying approximately 20 degrees of the cycle. *C* was a ripple potential generator (so-called "constant potential") having a tance. As will be shown, this is essential. The roentgen tube was of the Coolidge type, having thin walls. Since tubes of the same design vary slightly, a single tube was left in position for the six months dur-

of atmospheric air at 0°C. and 76 cm. mercury pressure such a degree of conductivity that one electrostatic unit charge is measured at saturation current.

[4] The "percentage depth dose" is the ratio of the roentgen-ray intensity as measured at a given depth in a body of homogeneous material, to the intensity as measured at the irradiated surface. It must be recognized that these intensities are measured in terms of roentgens per minute and hence do not give true indications of the energy absorbed in a given volume element.

[5] Up to the present the term "constant potential" has been used indiscriminately in describing the potential supplied by kenotron or other valve tube rectification. We will use a more accurate designation of voltages which are actually not constant but fluctuate about a certain average value. We thus define a "ripple quantity" (potential or current) as a simple periodic quantity $y=V_0+V_1 \sin(\omega x+\alpha_1)+V_2 \sin(2\omega x+\alpha_2)+\cdots$ in which the constant term (V_0) is so large that all values of the quantity are positive (or negative). The amount of ripple ("ripplage" or "ripplance") is a ripple quantity is the ratio of the difference between the maximum and minimum values of the quantity to the average value.

ing which the measurements were made. It was inclosed in a rectangular 1/4 inch lead box, 4×4×7 feet, and having forced ventilation. Previous experience indicated that roentgen tubes operate more smoothly in unconfined space than in some of the conventional tube drums. For example, it was found that for a tube operating at 200 kv. (peak) a spacing of about 12 inches from center to ground wall produced unsteadiness, whereas an 18-inch spacing appeared sufficient to avoid such difficulty. Accordingly, we used the 24-inch spacing and had no difficulty with tube unsteadiness at voltages up to 230 kv. (peak).

Control of the tube with generators *A* and *B* was observed by means of a d.c. milliammeter in the high tension circuit and a wide scale voltmeter connected directly across the transformer primary. Duplication of results over a period of months indicated that this control method was sufficient. In the case of the generator *C* ("constant potential") the control was

Table I

H-V.L.	Percentage Depth Dose		Ratio
mm. Cu	A	B	A/B
2.00	52	30	1.73
1.6	51	30	1.70
1.0	50	29	1.72
0.8	48	28	1.72
0.6	47	27	1.74
0.4	40	24	1.67
0.2	28	16	1.75
0.1	16	9	1.78
0.05	7	4	1.75

Relationship between radiation quality and percentage depth dose for two different field areas.
A—Field area 400 sq. cm; B—Field area 50 sq. cm.

Table II

Intensity	λ_e	H-V.L.	Abs. Curve	*A*	*B*	*C*
				KV. (Peak)	KV. (Peak)	KV. (av.)
	A	*mm. Cu.*				
215	—	—	—	*237	200	152
—	—	—	X	(215)	200	(155–60)
178	—	—	—	200	189	142
—	—	—	X	200	(190)	(150)
—	—	0.775	—	200	195	161
—	0.192	—	—	200	195	159
151	—	—	—	173	180	132
—	—	—	X	(180)	180	(135–40)
—	—	0.68	—	178	180	147
—	0.199	—	—	177	180	146
122	—	—	—	154	160	122
—	—	—	X	(150–55)	160	(125–30)
—	—	0.60	—	153	160	124
—	0.208	—	—	154	160	126
80	—	—	—	138	140	99
—	—	—	X	(135–40)	140	(105–10)
—	—	0.525	—	132	140	112
—	0.218	—	—	134	140	110

* Extrapolated value—probably too high.

Table giving potentials of generators *A*, *B* and *C* required to produce equal roentgen-ray intensities or qualities.

effected by means of a shielded high-tension voltmeter[6] connected directly across the tube leads.

Peak voltage was measured with a sphere gap in all cases. Average voltages were measured by means of the high-tension voltmeter, which in the case of *A* was so arranged that its phase position could be readily changed. The positions of the switches were at the points set by the agents of the respective manufacturers—presumably best suited for use at 200 kv. (peak).

Ionization measurements were made

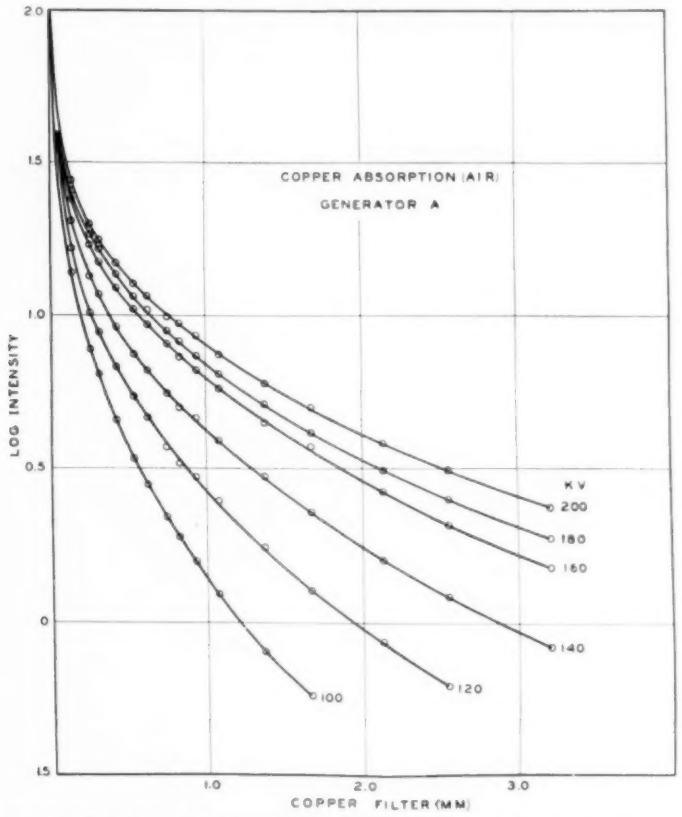


FIG. 4. Semilogarithmic copper absorption curve for generator *A*.

generator *C*, gave readings very slightly less than those of the sphere gap, depending upon the tube current. Since the rectification characteristics of generators *A* and *B* vary with load, this was kept constant at 4 ma. (av.) throughout the entire work.

The rectifying switch of generator *B* was fixed in a permanent position on the synchronous motor shaft, so measurements made with *B* were arbitrarily chosen as a basis in comparing with *A*. The switch on

[6] Taylor, L. S. *Bur. Standards J. Research*, 1930, 5, 609 (RP 217).

with a calibrated thimble ionization chamber arranged according to the diagram in Figure 1. The distance from focal spot to center of the chamber was 104 cm. The ionization chamber system was tested for leakage by covering the thimble chamber cap with lead and then exposing it to the roentgen beam. No leakage was detectable in an exposure time double the longest used in the measurements.

For depth dose measurements a cubical wax phantom about 35 cm. on a side was used. Wax was selected instead of water largely for convenience since its difference

from water has been shown[7] to be of no significance. The wax was carved out so that the chamber in the surface position was half submerged leaving no air pockets between it and the wax. The focal spot-surface distance was likewise 104 cm. A field area of 10 cm. diameter (78 sq. cm.) was chosen in order to work with a clearly defined beam receiving little stem radiation. Table 1 from Grebe and Nitzge shows that within wide limits depth dose variations with quality are independent of the field area.

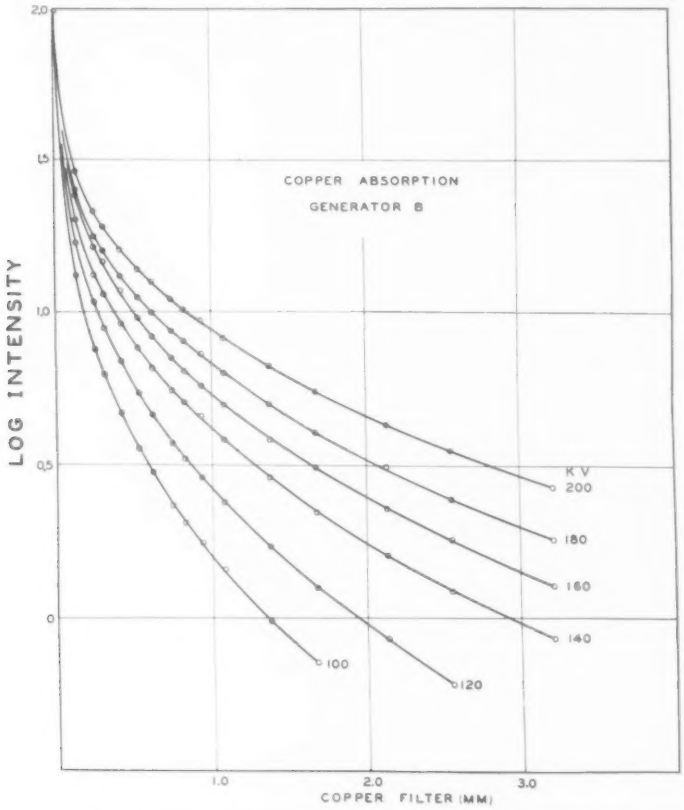


FIG. 5. Semilogarithmic copper absorption curve for generator *B*.

III. INTENSITY MEASUREMENTS IN AIR

The curves in Figure 2 give for generators *A* and *B* the beam intensity measured in air (in arbitrary units) as a function of the copper filtration in the beam. Each curve is for a constant peak voltage as measured with a sphere gap. It will be noticed that, for the same tube current and 200 kv. (peak), generator *B* gives about 20 per cent more radiation than *A* while at 180 kv. (peak) both are about the same. At 160 kv. (peak) *A* has a greater roentgen-ray emission than *B* and from 140 kv. peak down both are essentially the same.

Figure 3 gives a similar set of curves for generator *C* where the voltages are expressed in kilovolts average. The curve for 150 kv. (average), replotted as the broken line on Figure 2, approximates very closely the curve for 200 kv. (peak) on generator *B*. Similarly it will be found for the conditions used here that the other approximate intensity equivalents given in Table II are obtainable for radiation filtered through 0.5 mm. of copper.

[7] Grebe, L., and Nitzge, K. Tabellen zur Dosierung der Röntgenstrahlen. Sonderbände zur Strahlentherapie. (Hans Meyer, editor). Band XIV. Urban and Schwarzenberg, Berlin, 1930.

Thus to obtain a roentgen-ray intensity of 178 units from any of the three generators, through 0.5 mm. copper filter, would require that *A* be operated at 200 kv. (peak), *B* at 189 kv. (peak) and *C* at 142 kv. (av.). This is of course for the same tube current in all cases. Similarly an intensity of 80 units is obtained at 130 kv. (peak), 140 kv. (peak) and 99 kv. (av.), respectively.

To obtain some quantitative idea of the effect of shortening the aerial system, a section about 12 feet long was disconnected. This reduced the capacitance of the high-tension system by about a third (from 158$\mu\mu$f to 110$\mu\mu$f) and caused a noticeable decrease of the roentgen-ray emission at the higher voltages and a slight increase at lower voltages. It is thus shown clearly that had two different aerial systems been used comparisons between the two machines would have been grossly misleading, favoring one machine at higher voltages and the other at lower voltages.

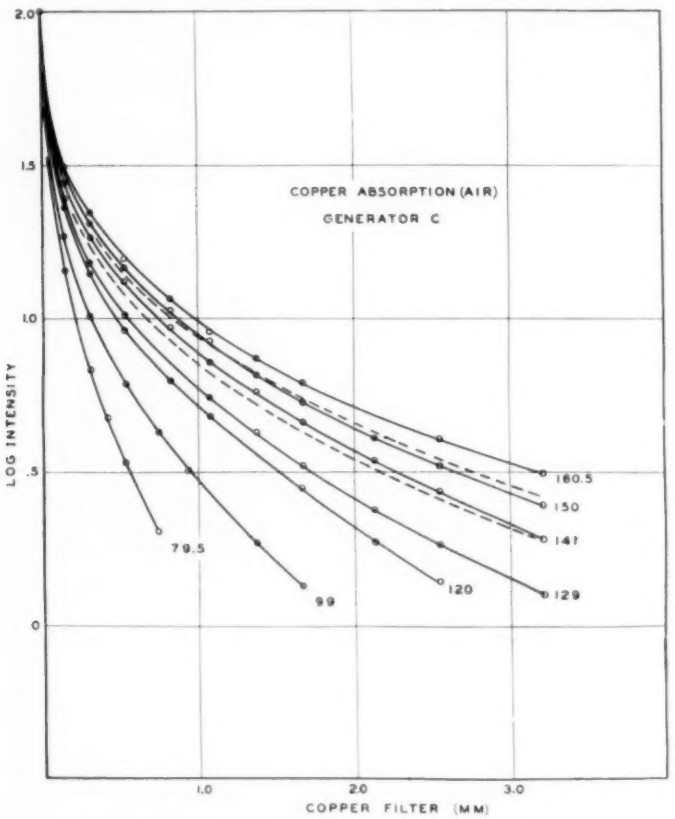


FIG. 6. Semilogarithmic copper absorption curve for generator *C*. Upper broken line curve for generator *B* at 200 kv. Lower broken line curve for generator *A* at 180 kv.

IV. QUALITY MEASUREMENTS IN AIR

It is believed that at present the most nearly adequate method of expressing the quality of a roentgen beam is to give its full absorption curve in copper or aluminum.[8,9] This is best done by plotting the logarithm of the intensity (or the percentage transmission) as a function of the filtration. It is not possible by this method

[8] Pohle, E. A., and Wright, C. S. Limit exposure in radiography; supplementary report. *Radiology*, 1930, *14*, 17–23.

[9] Wilsey, R. B. On specification of x-ray quality. *Radiology* 1931, *17*, 700–713.

to express a radiation quality as a single numerical magnitude.

For two radiation qualities to be equivalent, the curvatures of their respective absorption curves must be coincident. Where two curves do not exactly coincide, the difference in quality must be estimated. Wilsey has shown, however, that actual or estimated matching of absorption curves permits the most accurate reproduction of a given roentgen-ray quality.

One of the advantages of giving a full absorption curve is that all other quality expressions such as the half-value layer or effective wave length may be obtained from it. The slope of such a curve at any point gives the effective absorption coefficient of the radiation corresponding to the particular filter for which the point was chosen, and from this in turn may be obtained the true effective wave length of the beam.[10]

Figures 4, 5, and 6 give the copper absorption curves for generators *A*, *B*, and *C*, respectively. These curves are from the same data used for Figures 2 and 3. It is significant to note that the 200 kv. (peak) curve for generator *B* indicates a generally more penetrating radiation than for generator *A* at the same voltage. At 180 kv. (peak) the qualities are about the same, while at 150 kv. (peak) the reverse obtains. From 140 kv. (peak down, the qualities are again roughly the same. In other words, as shown in Table II, the qualities of the radiations bear a similar relationship to

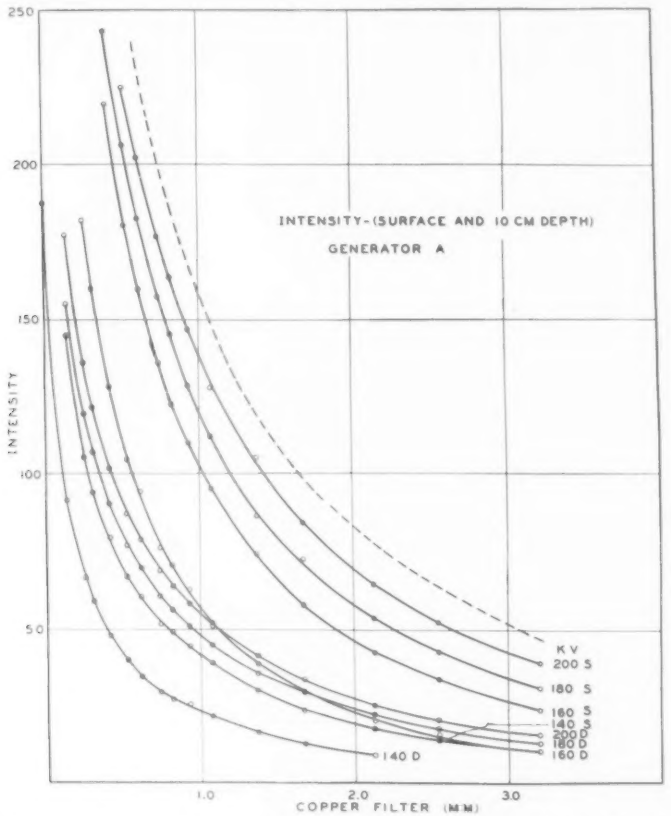


FIG. 7. Beam intensities for generator *A* measured at phantom surface (*S*) and at 10 cm. phantom depth (*D*). Broken curve is for 200 kv. on generator *B* measured at surface.

[10] Taylor, L. S. *Bur. Standards J. Research*, 1930, *5*, 517. This corresponds to Mutscheller's "average wave length."

one another as do the intensities, so that, for a given peak voltage, and a given filtration, if the radiation emission of *A* is greater than *B* for the penetration of *A* is likewise greater than *B*. It is unsafe to draw any generalization from these results other absorption curves for the different generators and we find that Table II above for intensity equivalents holds approximately true for quality equivalents also.

Depth Dose Measurements. Measurements of the percentage depth dose were

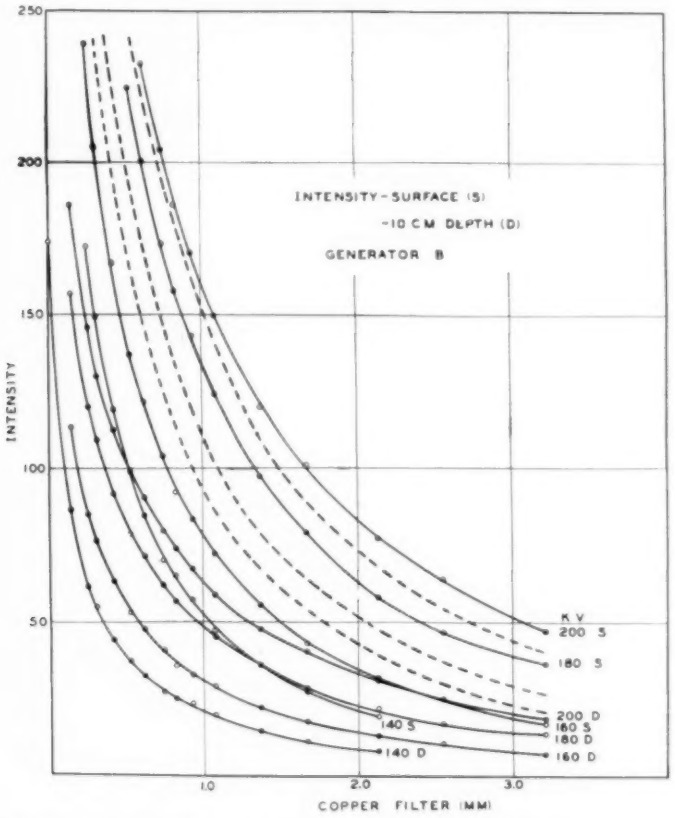


FIG. 8. Beam intensities for generator *B* measured at phantom surface (*S*) and at 10 cm. phantom depth (*D*). Broken line curves (top to bottom) for same generator except with shortened aerial operating at 200, 180, and 160 kv. (peak).

but it may be noted that such is roughly the case for all conditions thus far encountered in this work.

In Figure 6, giving the copper absorption curves for generator *C*, the broken lines are transposed from Figures 4 and 5. It will be noted that the 200 kv. (peak) curve for generator *B* (upper broken curve) corresponds very nearly in slope to the 150 kv. (av.) curve for generator *C*. (It will be recalled that the corresponding intensity curves also nearly coincide.) Similarly, it is found possible to match the

made over the whole range of radiation qualities used. Figures 7, 8, and 9, give respectively the surface and 10 cm. depth intensities for generators *A*, *B* and *C*. Comparison of the curves for the two mechanical rectifiers shows the same general similarities as were evidenced by the air intensity curves given in Figures 2 and 3. Thus the 200 kv. curve for generator *B* (broken line curve in Fig. 7.) shows a considerably greater surface dose than the 200 kv. curve for generator *A*.

Again the intensities measured at 10 cm.

depth for the two machines are related in the same manner as the air intensities.

The broken line curves in Figure 8 are intensities for generator *B* when used with the shortened aerial system. As noted for the air intensity measurements, the long aerial system has a greater roentgen-ray emission at 200 and 180 kv. and a smaller emission at 160 kv. than the short aerial system. Below 160 kv. there appears to be no significant difference between generators.

In comparing generator *C* with *A* and *B*, it is found (Fig. 9) that 160.5 kv. (av.) on *C* produces slightly greater air and surface intensities than 200 kv. (peak) on generator *B* while 150 kv. (av.) on *C* is about equivalent to 200 kv. (peak) on generator *A*. Also 140 kv. (av.) on *C* is seen to be equivalent to 180 kv. (peak) on either *A* or *B*.

Quality measurements as here carried out, with the thimble chamber at the phantom surface and at 10 cm. depth, have no real significance in relating the radiation quality in a phantom to that in air. This is because radiation under such conditions contains a major proportion of very soft scattered roentgen rays that introduce a large and unknown wall correction into the measurements. Since it is impossible to reproduce such radiations entering a standard chamber, the thimble chamber cannot be calibrated for equivalent radiation qualities.

Such curves have significance, however, in comparing radiation qualities measured under identical experimental conditions and as such have been used to compare depth dose qualities.

Figures 10, 11, and 12 give the copper absorption (corresponding to the intensity

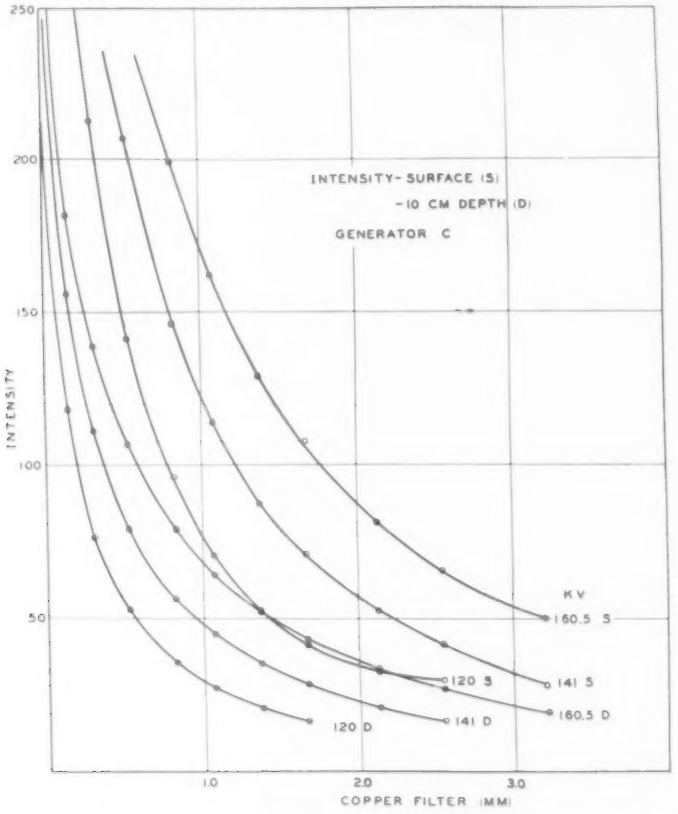


FIG. 9. Beam intensity for generator *C* measured at phantom surface (*S*) and at 10 cm. phantom depth (*D*).

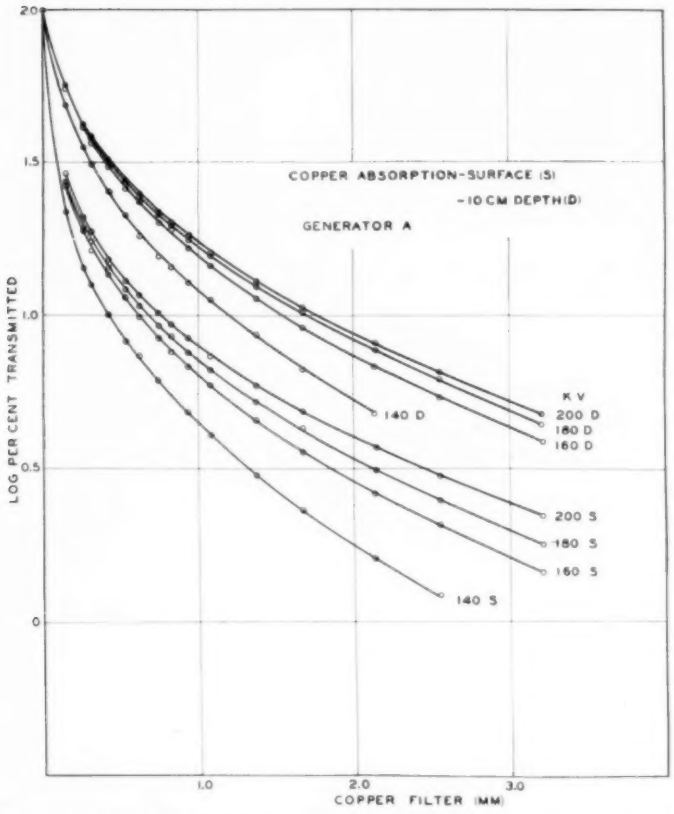


FIG. 10. Semilogarithmic copper absorption curves for radiation measured at surface (*S*) and 10 cm. depth (*D*) on phantom for generator *A*.

TABLE III

Filter mm. Cu	kv. (peak)		kv. (Av.)	kv. (peak)		kv. (Av.	kv. (peak)		kv. (Av.
	200	200	160.5	180	180	140	160	160	120
	A	*B*	*C*	*A*	*B*	*C*	*A*	*B*	*C*
0	18	18	—	17	16	—	16	16	—
0.14	35	34	34.8	34	31	34.2	34	33	29.3
0.304	—	—	36.9	—	—	37.5	—	—	35.9
0.415	37	38	—	37	35	—	37	38	—
0.6	38	38	38.3	37	37	38.4	37	39	37.7
0.8	38	39	—	38	37	—	39	39	—
1.0	38	39	40.0	38	37	38.9	40	39	—
1.5	39	40	—	39	38	—	40	40	38.7
2.0	39	40	41.3	40	38	40.4	40	39	—
2.5	38	39	—	38	37	—	40	40	—
3.0	39	39	—	40	38	—	—	—	40.0

Percentage depth doses in wax phantom (field 10 cm. diameter) for different copper filtrations. (Letters at top of columns refer to generators.)

curves of Figures 7, 8 and 9) measured at the surface and 10 cm. depth for generators *A*, *B*, and *C*, respectively. On the assumption that similar absorption curves, obtained under identical conditions, imply equivalent radiations, these curves show

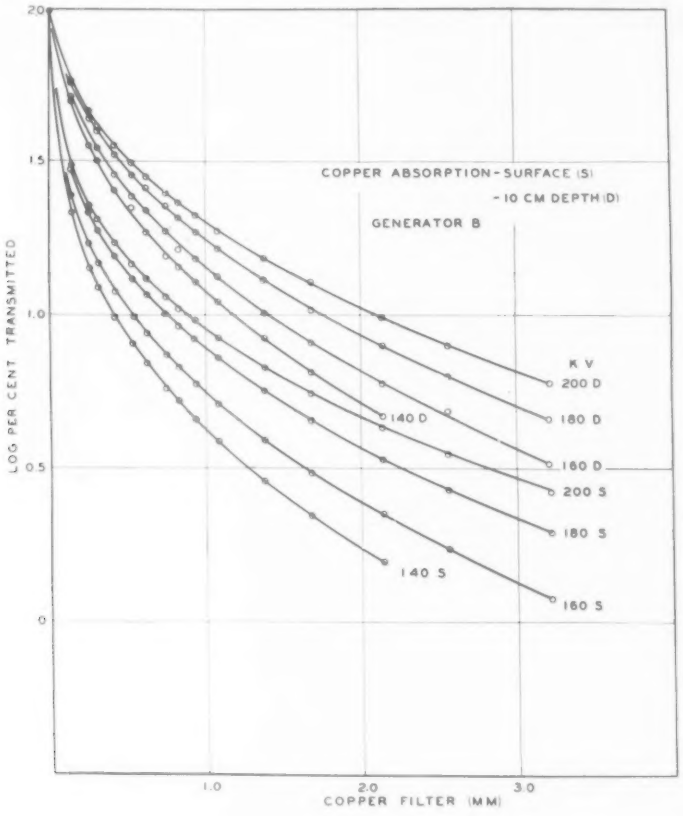


FIG. 11. Semilogarithmic copper absorption curves for radiation measured at surface (*S*) and 10 cm. depth (*D*) on phantom for generator *B*.

precisely the same relation between the 10 cm. depth radiation qualities for the three generators as was indicated by the absorption curves measured in air.

Percentage depth doses for all the conditions here used may be obtained directly from the curves in Figures 7, 8 and 9. It happens that the percentage depth dose changes but very slowly with increasing hardness of radiation after 0.1 or 0.2 mm. copper filtration. It also changes but slightly with increase of voltage above 160 kv. (peak). Consequently the change in percentage depth dose is an insensitive indicator of radiation equalities. It cannot, however, be neglected; since, if two radiations, having otherwise similar properties, should differ materially in percentage depth dose, there would be no justification for saying that they were equivalent.[11]

The change of depth dose with filtration for the three generators is given in Table III. It is seen that, while the accuracy is none too good, the percentage depth doses with generators *A* and *B* are about the same at equal voltages. The depth doses

[11] It should be noted that a percentage depth dose is the ratio between two measurements and hence its error may be considerably larger than the individual errors of the original measurements.

at 160 kv. appear to be slightly greater than at higher voltages which is probably unreasonable but may be due to small cumulative errors. In comparing generator *C* with the mechanical rectifiers, it is found that the depth doses at 160 kv. (av.) for *C* slightly exceed those at 200 kv. (peak) for *A* and *B* and likewise the depth doses at 140 kv. (av.) for *C* are slightly greater than those at 180 kv. (peak) for *A* and *B*. At 160 kv. (peak) generators *A* and *B* give a slightly greater depth dose than *C* operating at 120 kv. (av.). The importance of these depth dose measurements rests in their agreement and no inference should be drawn from the small differences found.

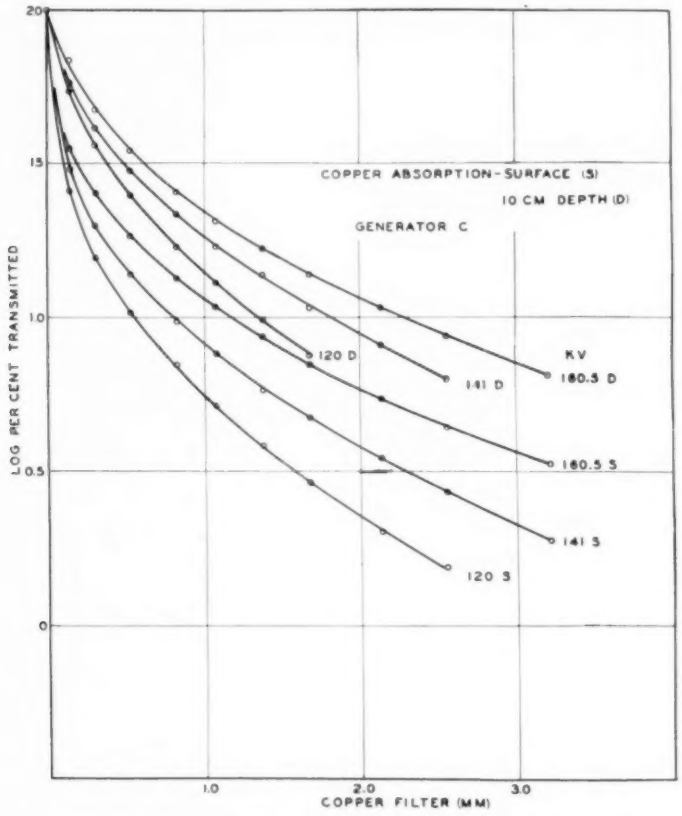


FIG. 12. Semilogarithmic copper absorption curves for radiation measured at surface (*S*) and 10 cm. depth (*D*) on phantom for generator *C*.

VI. HALF-VALUE LAYERS AND TRUE EFFECTIVE WAVE LENGTHS

The results above have shown that the copper absorption curves for the three generators give a fairly reasonable comparison of the resulting tube emission as regards quantity, quality and depth dose From the curves given, effective wave lengths or half-value layers in copper for any desired beam of radiation may be obtained directly. In practice, radiation qualities have been variously expressed by either of these two methods. Hence, for facilitating comparisons of the radiation output of generators, values of the copper half-value layer (H-V. L.) and true effective wave length (λ_e), covering all the

radiations used in this study, have been plotted in Figures 13 and 14. It should be emphasized that the values for mechanical rectifiers are likely to vary somewhat between machines and that the values here given hold strictly only for our generators. They should, serve as a fairly close guide.

Values of H-V. L. and λ_e also depend upon the thickness of the tube wall, this probably accounting for the differences in

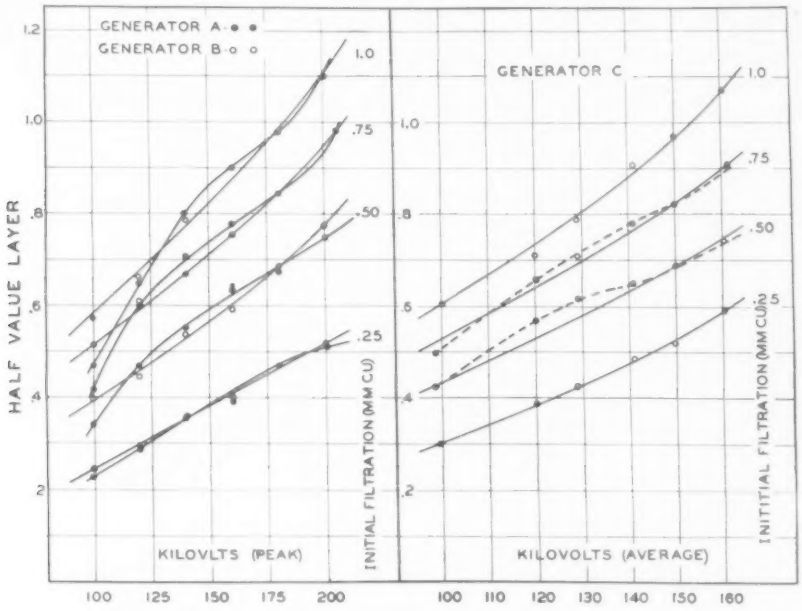


FIG. 13. Half-value layer curves for generators *A*, *B* and *C*.

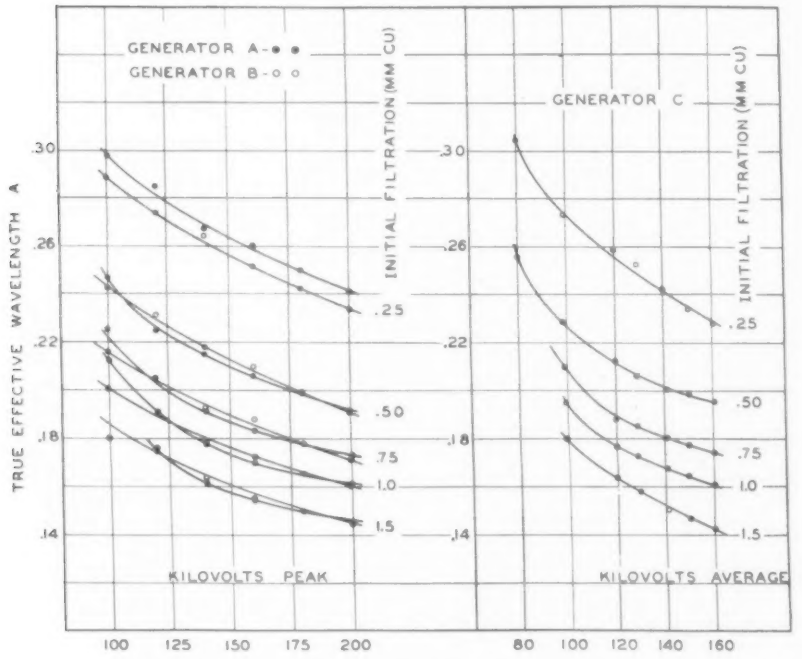


FIG. 14. Effective wave length curves for generators *A*, *B* and *C*.

H-V. L. for "constant potential" reported by several workers. Probably a more serious source of difference between workers lies in their method of voltage measurement and in the amount of ripplage present in their generators. When using generator *C* ripplage was found to be about 8 per cent and to vary slightly with voltage. Voltage measurements were made by means of a shielded high resistance "voltmeter multiplier" in series with a d.c. microammeter.[12] Thus the potentials are expressed in average kilovolts whereas the potentials used by other workers in measuring the half-value layer were usually, if not always, in peak kilovolts. To show how various observers agree, their results are plotted in Figure 15. There appears to be no systematic difference except that Holthusen's are consistently higher than all others. Our measurements fall between the others over a large portion of the range covered.

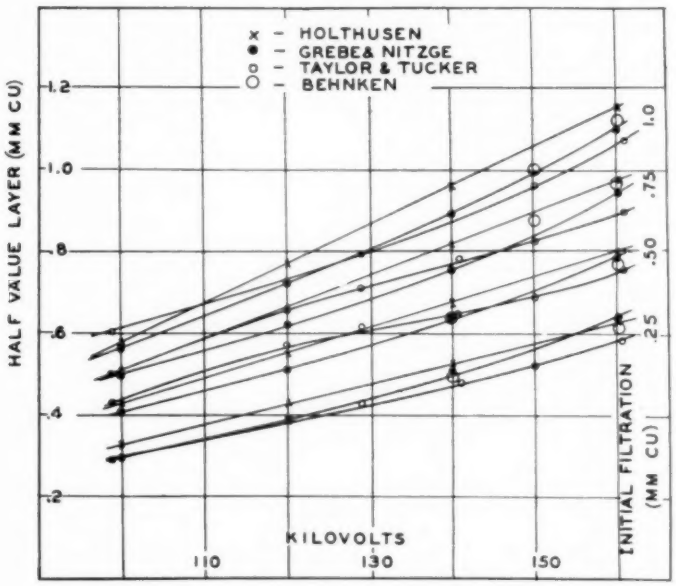


FIG. 15. Comparison of half-value layer measurements by different observers.

The "quality" comparisons of the three generators, made from the full absorption curves, are borne out very well by the H-V. L. and λ_e curves of Figures 13 and 14. For example, a roentgen beam, filtered with 0.5 mm. copper and having a H-V. L. of 0.75 mm. Cu, may be obtained with 200 kv. on generator *A*, 195 kv. on *B*, and 160 kv. on *C*. Again a beam filtered with 0.25 mm. copper and having a H-V. L. of 0.50 mm. copper may be obtained with 210 kv. on *A*, 202 kv. on *B*, and 150 kv. on *C*. We find a similar relationship from the effective wave length curves. Thus a beam filtered with 0.5 mm. Cu and having a value of $\lambda_e = 0.195$ Angström may be obtained with 200 kv. on *A*, 196 kv. on *B*, and 160 kv. on *C*. Again a 0.25 mm. copper filtered beam having $\lambda_e = 0.235$ Angström is obtained by 212 kv. on *A*, 203 kv. on *B* and 150 kv. on *C*. The agreement of these with the results obtained from the H-V. L. curves is probably within the experimental error.

VII. VOLTAGE MEASUREMENTS

A partial explanation, at least, for the variation in roentgen-ray emission under

[12] See footnote No. 6.

apparently identical conditions, is found to lie in the method of voltage measurement. The emission of a roentgen tube operating on a mechanically rectified generator depends upon the wave form of the voltage and the voltage-space current characteristic of the tube. If the tube current saturation is reached at a comparatively low voltage, then the voltage wave form of the generator is the predominant factor in determining the tube output. The wave form in turn depends upon current load drawn from the generator, the voltage and the setting of the rectifying switches. It happens that in general no single setting of the rectifiers will suffice to yield the maximum output for all current and voltage combinations. In practice a single rectifier setting is used for all operating conditions and as a consequence the optimum output is realized only for a narrow range of conditions.

In measuring the voltage with a sphere gap the peak of the wave is the quantity determined, regardless of the wave form. Thus while the peak voltage of two waves may be the same, if one is a sharp-topped wave form while the other is broad-topped, it is obvious that the tube output for the latter will exceed that of the former. This condition may be largely met if the generator output voltage be measured in *effective* rather than peak kilovolts.

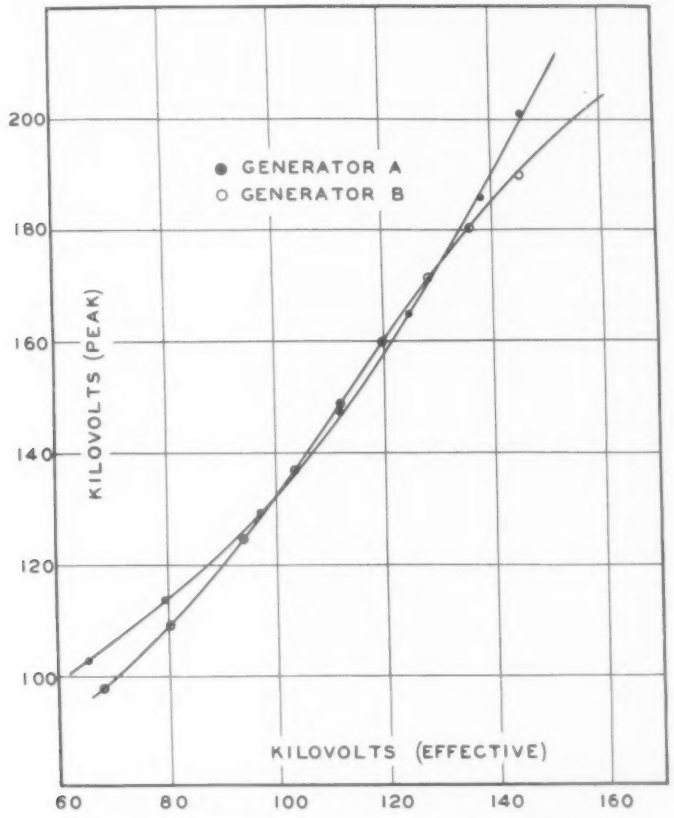


Fig. 16. Effective and peak voltage measurements on generators *A* and *B*.

This was readily accomplished by means of the high voltage voltmeter described in conjunction with the constant potential generator. As used up to the present, the 150 megohm non-induction shielded re-

sistor[13] was in series with a d.c. microammeter and thus measured *average* voltage. When the d.c. instrument is replaced by an a.c. microammeter the potential is measured in *effective* kilovolts. In this work, the latter instrument not being readily available, we used a Kelvin multicellular electrostatic voltmeter to measure the potential drop across 75,000 ohms placed in series with the main high resistance. The meter then read the voltage across the line.

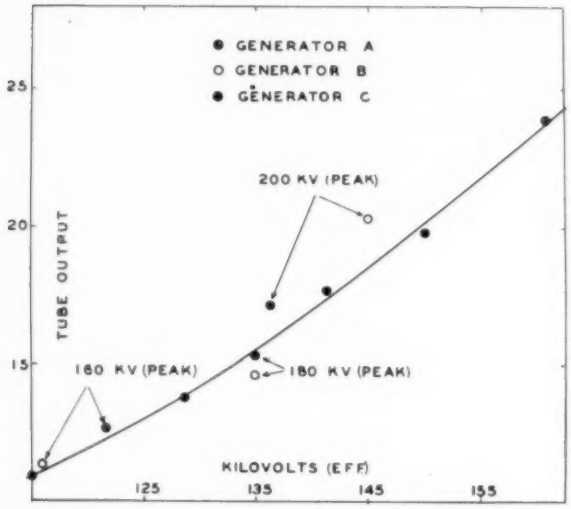


FIG. 17. Plot showing tube output as a function of effective voltage for generators *A*, *B* and *C*.

In the case of generator *C* the effective and average voltages are nearly identical. However, for mechanically rectified potentials, the effective voltage is considerably higher than the average. Figure 16 shows the relation between the peak and effective voltage for generators *A* and *B* used in this study. In order to produce the same total load on the rectifier as used in the previous experiments—thus having nearly the same wave form—the tube current was adjusted so that when added to that through the voltmeter (0-1 ma.) the total was 4 ma. Curves *A* and *B* are for generators *A* and *B*, respectively, whence it may be seen that for the same peak voltage the two systems have quite different effective voltages.

That the effective voltage is more closely related to tube output than peak voltage may be readily seen. For example, for the same 200 kv. peak, generator *B* had a greater output; and, as seen in Figure 16, the effective voltage of *B* exceeded that of *A*. Similarly at 180 kv. (peak) the outputs were approximately equal and it is likewise found that the effective voltages were about the same, and so on.

To compare the output of the three generators, when the potential is measured in effective kilovolts, the curve in Figure 17 shows the relationship between the beam intensity (filtered through 0.525 mm. of copper) and the effective kilovoltage. Curve *C* is for generator *C* ("constant potential") and the other points are as indicated. It is seen at once that the output at a given voltage is of the same order of magnitude for all three generators. Since the radiation quality was found to be roughly proportional to the intensity for a given tube current, it follows that the effective voltage also presents a fairly close indication of the quality. These results will be discussed in greater detail in a later paper.

CONCLUSIONS

It is believed that any value to be ascribed to this study lies in showing physical similarities, and not differences, between high voltage roentgen-ray generators. Care has been taken to avoid any comparisons of the biological effectiveness per se of the radiations used. One of the outstanding biological problems is how to administer a desired dose of radiation within the body without at the same time producing a dangerous skin erythema or destroying intervening tissue. It has been shown here how equivalent depth doses may be obtained with different generators and a wide range of qualities and intensities. The clinical application of this

[13] These have been described in the paper referred to in footnote No. 6. It was found that the separate units making up the final resistor had a very slight negative impedance at 1000 cycles.

wide range of radiations depends on two factors which must be decided by the clinician, not by the physicist. The first is the relationship between quality and the erythema dose; the second is the economics of administering radiation,[14] for obviously it would not be economical to use highly filtered low voltage radiation for deep therapy when there is available a much greater intensity of less filtered radiation—assuming the biological effect to be the same.

[14] Failla, G. *Dissert. l'Univ. de Paris*, Serie A, No. 1776, 1923.

It is hoped that the results of the present study will enable the clinician to better compare his technique with that of others using different generators and making his measurements by different methods.

This study has been made possible through the support and generous cooperation of the Radiological Research Institute and roentgen-ray manufacturers of this country, for which we express our appreciation. In addition, we thank Messrs. G. Singer and C. F. Stoneburner of this laboratory for their assistance, particularly with the effective voltage measurements.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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For Preliminary Program of American Congress of Radiology: See April Number, AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY, page 539.

Date of Meeting: September 25–30, 1933.

Place of Meeting: Palmer House, Chicago, Ill. Scientific Sessions, Scientific and Commercial Exhibits will all be held in this Hotel.

* For Officers and Standing Committees of the American Roentgen Ray Society and the American Radium Society usually carried on this page, see the April, 1933, number of the Journal.

† Combined meeting of: American Roentgen Ray Society, American Radium Society, American College of Radiology, Radiological Society of North America.

EDITORIAL

PITUITARY BASOPHILISM
(CUSHING'S SYNDROME)

MEDICAL publications naturally fall into two groups: original and second-hand communications. The latter form by far the larger part of our medical literature, and with the exception of textbooks, where the material is valuable, it is largely a waste of space, not to mention the time of the intelligent reader. Original work, on the other hand, although rare, is priceless and deserves the accord which it usually receives. Most of the original medical papers are *analytical* in that they consider a group of cases roughly similar and then by one means or another split off from the main group a smaller one presenting a definite clinical syndrome or a particular phase of a syndrome and thus the author creates a further subdivision of diagnosis or therapy, as the case may be. A rarer form of original medical thinking and writing is the type which might be called "*synthetic*," in that the author puts together a divergent group of cases, or patients with dissimilar symptoms, and, like putting together the pieces of a jig-saw puzzle, makes a harmonious whole out of uncertain or apparently unequal parts.

Some writers are known for their relatively unimportant reviews of other authors' contributions; a few are known for a single outstanding contribution to their field of knowledge, aside from which they have been sterile. Rare indeed is the physician who produces many valuable and original works in a lifetime, but a few there are, and one almost comes to expect at least an annual gift of knowledge from such a writer.

Of such material, original and in a sense synthetic, are the recent papers by Cushing* on the basophilic adenomas of the pituitary body. He establishes a new syndrome, demonstrates the probable cause, shows the means whereby it works, and gives a hint as to possible treatment. As usual he seizes upon facts and conditions which should have been apparent to everyone, beginning his observations upon the patient and ending in the laboratory,—the course of most original and valuable aids to clinical medicine. From these he pursues a line of clinical reasoning and then draws his conclusions and puts forth his theory, rather than starting with a theory or beginning in the laboratory and then hunting for patients to fit the established mold.

In this particular case Cushing, in his second paper, describes a group of patients, fourteen in all, the majority of whom were young women with a peculiar plethoric adiposity of the face, neck and trunk but sparing the extremities. Associated with this peculiar and often painful adiposity are a group of symptoms and conditions which may well be classed as "polyglandular." Most of the female patients have hypertrichosis, particularly noticeable on the face and neck, with thinning of the normal hair. They also have amenorrhea, and are extremely asthenic, often with a low basal metabolic rate, averaging −28. Strikingly frequent is an otherwise unexplained vascular hypertension, above 200 mm. of mercury in some cases, and a polycythemia which may reach 7 or 8 million red blood cells per cubic millimeter. The abdomen and thighs of these patients, less commonly their arms, may show striae distensae identical with those seen on the abdomen of a

* Cushing, H. The basophil adenomas of the pituitary body and their clinical manifestations (pituitary basophilism.) *Bull. Johns Hopkins Hosp.*, 1932, *50*, 137–195.

Cushing, H. Further notes on pituitary basophilism. *J. Am. M. Ass.*, 1932, *99*, 281.

pregnant woman. The skin of the extremities is apt to be dry and parchment-like, sometimes mottled and blotchy, the so-called "cutis marmorata." Cyanosis of the acral parts is often marked, especially the hands and feet, and the skin bruises easily, frequently with multiple large subcutaneous hemorrhages. Pigmentation of the skin in unusual distributions may be found. Of interest to blood chemists and to those interested in diabetes is the frequent hyperglycemia, with diminished sugar tolerance and frequent periods of alimentary glycosuria. Of particular interest to roentgenologists is the softening of the skeleton which so often occurs, and which is demonstrable roentgenologically, with the usual changes subsequent to considerable loss of calcium, i.e., impaction of the vertebral bodies (with kyphosis and a decrease in the patient's height), occasional spontaneous fractures of the long bones, and generalized decalcification of the bones, particularly of the skull, vertebrae and pelvis, sometimes with a mottling somewhat suggestive of that following hyperparathyroidism. The degree of softening is noted in some of the autopsy records where it is stated that the cranial bones can easily be cut with a knife.

This whole polyglandular syndrome Cushing ascribes to the pituitary body, "the conductor of the endocrine orchestra," and the various abnormal states or conditions are supposed to be dependent upon the individual endocrine gland affected; for example, stimulation (?) of the parathyroids causes the abnormal calcium excretion with consequent softening of the skeleton; of the adrenals accounting for the hypertension, pigmentation and asthenia; of the gonads accounting for the changes in secondary sex characteristics; of the pancreatic islets to account for the hyperglycemia and the glycosuria, and either stimulation or suppression of thyroid function to account for the changes in basal metabolic rate. Not only does he place the responsibility for initiating these changes upon the pituitary body but he also identifies the cells at fault, in this case the less well-known and little understood basophile cells which form a small but extremely potent adenoma, often invisible to the naked eye. Roentgen examination of the skull in an attempt to demonstrate enlargement of the sella by a basophilic adenoma would therefore be useless; it would be the generalized decalcification and softening of the bones which would give the roentgenologist his first hint as to the underlying condition.

Cushing having established this condition as a clinical entity, largely through clinical observation and by collecting cases of polyglandular adiposity from the literature, it remained for one of his students, Dr. Teel, first to predict a basophilic adenoma subsequently confirmed at autopsy (Case 7). Thus again the prepared mind is enabled to appreciate the unusual and to exorcise the spirit of darkness which is born of mental blindness.

Of final interest to the roentgenologist is the suggestion that these tumors may repond to radiation therapy. The basophile cells are derived from the mother cell of the pituitary body, just as are the acidophilic cells, which are the potent factor in acromegaly. The latter are known to respond well to radiation therapy, and by à priori reasoning the basophile cells should also be affected in a similar manner. In one of the reported cases (Case 14) there is clinical evidence that this is true, with definite improvement following radiation therapy, but enthusiasm must be tempered with judgment, as tumors of the ductless glands have been known to undergo spontaneous remissions. Surgery can be of no avail because of the minute size of the tumor and because of its unpredictable location, so that radiation therapy seems to be the only recourse in the attempt to obviate the usual fatal result of these minute but extremely potent basophile adenomas of the pituitary body. It behooves roentgenologists therefore to be doubly watchful,—to assist in the proper recognition of these cases and to be prepared to administer the proper therapy with careful follow-up to throw more light on this rare but interesting clinical condition.

Merrill C. Sosman

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa.
Annual Meeting: Chicago, Ill., Sept. 25–30, 1933.

American College of Radiology
Secretary, Dr. Albert Soiland, 1407 S. Hope St., Los Angeles, Calif.
Annual meeting: Chicago, Ill., Sept. 25–30, 1933.

Section on Radiology, American Medical Association
Secretary, Dr. J. T Murphy, 421 Michigan St., Toledo, Ohio.
Annual meeting: Milwaukee, Wis., June 12–16, 1933.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y.
Annual meeting: Chicago, Ill., Sept. 25–30, 1933.

Radiological Section, Los Angeles County Medical Society
Secretary, Dr. D. R. MacColl, 2826 S. Hope St., Los Angeles, Calif.
Meets on the third Wednesday of each month at the California Hospital.

Radiological Section, Southern Medical Association
Secretary, Dr. C. H. Heacock, 20 S. Dunlap St., Memphis, Tenn.
Annual meeting: Richmond, Va., November, 1933.

Brooklyn Roentgen Ray Society
Secretary, Dr. G. W. Cramp, 921 President St., Brooklyn, N. Y.
Meets monthly on first Tuesday, October to April.

Buffalo Radiological Society
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y.
Meets second Monday of each month except during summer months, place of meeting selected by the host.

Chicago Roentgen Society
Secretary, Dr. George M. Landau, 660 Groveland Park.
Meeting second Thursday of each month October to May inclusive at Virginia Hotel.

Cincinnati Radiological Society
Secretary, Dr. H. G. Reineke, Christian R. Holmes Hospital, Cincinnati, Ohio. Meetings held monthly.

Cleveland Radiological Society
Secretary, Dr. M. A. Thomas, Medical Arts Bldg.
Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital.
Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

Florida Radiological Society
Secretary, Dr. W. McL. Shaw, 418 St. James Bldg., Jacksonville, Fla.
Meetings held twice a year, May and November.

Illinois Radiological Society
Secretary, Dr. L. M. Hilt, Myers Bldg., Springfield, Ill.
Regular meetings held quarterly.

Indiana Roentgen Society
Secretary, Dr. J. N. Collins, Indianapolis, Ind.
Annual meeting each February 22 in Indianapolis.

Michigan Association of Roentgenologists
Secretary, Dr. S. W. Donaldson, St. Joseph's Mercy Hospital, Ann Arbor, Mich. Three meetings a year, Fall, Winter, and Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. J. E. Habbe, 221 Wisconsin Ave., Milwaukee, Wis.
Meets first Friday in October, December, February and April. Place of meeting designated by the president.

Minnesota Radiological Society
Secretary, Dr. L. G. Rigler, University Hospital, Minneapolis, Minn.

New England Roentgen Ray Society
Secretary, Dr. Thomas R. Healy, 370 Marlboro St., Boston, Mass.
Meets monthly on third Friday, Boston Medical Library.

New York Roentgen Society
Secretary, Dr. C. W. Schwartz, 33 E. 68th St., New York.
Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

Central New York Roentgen Ray Society
Secretary, Dr. H. S. Bull, 604 Masonic Temple, Auburn, N. Y.
Three meetings a year—January, May and November.

Pennsylvania Radiological Society
Secretary, Dr. W. E. Reiley, Clearfield, Penna.
Annual Meeting, Penn-Alto Hotel, Altoona, Pa., May 24–25, 1933.

Philadelphia Roentgen Ray Society
Secretary, Dr. Karl Kornblum, 3400 Spruce St.
Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thomson Hall, College of Physicians, 19 S. 22d St.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. W. W. Fray, Strong Memorial Hospital.
Meets monthly on second Thursday from October, 1932, to May, 1933 inclusive, at 7:45 at the Rochester Medical Association Building.

St. Louis Roentgen Club
Secretary, Dr. W. K. Mueller, University Club Bldg.
Meets first week of each month. Time and place of meetings designated by president.

South Carolina X-Ray Society
Secretary: Dr. R. B. Taft, 105 Rutledge Ave., Charleston, S. C.
Meets at time and place of South Carolina State Medical Association.

Texas Radiological Society
Secretary-Treasurer, Dr. C. P. Harris, Houston, Texas.
Meets annually one day preceding the meeting of the Texas State Medical Association.

University of Michigan Roentgen Ray Society
Secretary, Dr. C. C. Taylor, University Hospital, Ann Arbor, Mich.
Meets first and third Wednesday evening of the month from October to June, at 8 o'clock in the amphitheatre of the University Hospital.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Virginia Roentgen Ray Club
Secretary, Dr. Wright Clarkson, 205 S. Sycamore St., Petersburg, Va.
Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Luis Fariñas, Animas 110, Havana, Cuba.
Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1., or as advertised.

Electro-Therapeutic Section of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:30 P.M. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Colin Macdonald, Lister House, 61 Collins St., Melbourne, Australia.
Meets monthly at Melbourne during the winter.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. H. Rolph, 160 St. George St., Toronto, Ont.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Allies, 134, Louvain, (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Societe de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11/52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April in different German cities, at least once in five year in Berlin. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Maracine 30 Bucarest, Rumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR, in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson.
Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology of Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. H. Scheuermann, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Society of Roentgenology
Meets first Tuesday each month, October to July.

Orient

Japan X-ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike, Kyoto, Japan. Meets bi-monthly on third Sunday.

A NEW HONOR COMES TO DR. KÖHLER

At the recent annual meeting of the German Roentgen Society held at Bremen, which was attended by 1200 roentgenologists, the Rieder Gold Medal for extraordinary work in roentgenology was awarded to Professor Dr. Alban Köhler, Facharzt für Röntgenologie, Wiesbaden, Germany. This medal has been previously awarded only to Professor Holzknecht of Vienna, and Professor Gösta Forssell of Stockholm. Professor Köhler is an honorary member of the American Roentgen Ray Society and therefore this award is of interest to American roentgenologists. Professor Köhler has always been an outstanding investigator. His book, "Röntgenology: The Borderlands of the Normal and Early Pathological in the Skiagram" is an enviable achievement and has been most helpful to every roentgenologist, for it is the borderline diagnoses that are always the most difficult. It has passed through five German editions and has been translated into English.

Professor Dr Alban Köhler

Congratulations are due Professor Köhler.

George E. Pfahler

DEPARTMENT OF TECHNIQUE

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PROCEDURE IN THE ROENTGEN STUDY OF THE BREAST

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IT IS acknowledged to be true that it is not always possible to diagnose lesions of the breast by physical examination with the degree of accuracy necessary for a definite, therapeutic decision, particularly in the heavy, massive breast.

FIG. 1. Position of the patient.

A study of the breast by a roentgenographic method will demonstrate changes in the internal architecture of the organ not only in the normal, but also the pathological breast during the cycles of menstruation and pregnancy, and in tumors.[3,4] The following gives in more detail the roentgenographic technique in response to numerous inquiries:

In regard to the position during the roentgen exposure (Fig. 1), the patient is placed on her side with the affected breast nearest the surface of the table. The arm of this side is drawn up in abduction. Extreme abduction of the arm should be avoided, due to the fact that too great tension on the anterior and posterior axillary folds will cause a disarrangement of the architecture of the breast. In placing the arm in this position, the lateral borders of both the anterior and the posterior axillary folds are brought into exact vertical alinement with each other. This is done so that the relative density throughout the breast and axilla will be as nearly as possible the same. Considering the breast as a cone with its apex at the nipple and the base along the pectoral fascia, the patient is now in that position where the base of the cone is perpendicular to the film which was previously placed in the tunnel beneath the patient.

When a pendulous breast is being examined, a cradle (Fig. 2) is used to hold the organ perpendicular to the chest wall. This cradle is particularly necessary when the left breast is being examined, for any slight movement, even that caused by the impulse of the heart, is sufficient to blur the image.

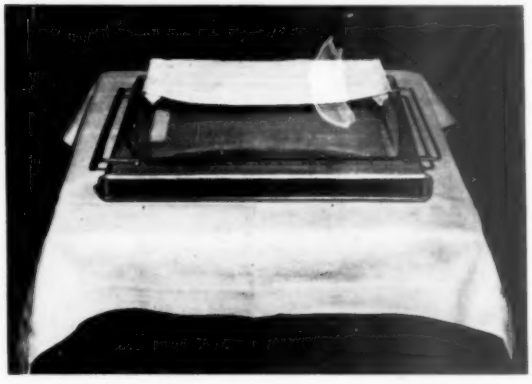

FIG. 2. Breast cradle.

The cradle consists of a steel frame with

a base 18×16 inches in size and in the shape of a U. Two inches toward the center from each end of the frame will be noted an elevated cross-member which is 1½ inches above the base. This cross-member acts as an abutment for the flexible gauze hammock that supports the breast during the roentgen exposure. In the preparation of this cradle the use of washed gauze is recommended. Unwashed gauze, with its starch and sizing, will in many instances cast a roentgen shadow.

Fixation of the patient is highly desirable and may be accomplished by the use of large sand bags (Fig. 3) placed along the dorsal spine. The roentgen tube is then centered with a target tube distance of 30 inches, on a line tangent to the wall of the thorax at the mid-clavicular line. This line will then be parallel to the base of the breast and perpendicular to the film surface. An exposure is made on double screens for one second with 30 ma. of current and a 2½ inch spark gap (measured between sharp points). The stereoscopic exposures[1] made in this way are also a great help in the roentgen interpretation of films of the breast.

The Potter-Bucky diaphragm is not used for two reasons; first, it increases the time of exposure, which in itself has been found to be disadvantageous, for in this particular instance it is desirable to have as short an exposure as possible in order to minimize the amount of movement, which is a great hindrance in studying the soft tissue details; secondly, the Potter-Bucky diaphragm is so constructed that its use in roentgenography of the breast will bring the film too far from the breast and so cause a distortion in size and shape of the breast architecture.

It is recommended that a roentgenogram be made of both the suspected and the normal breast, as well as both axillary areas. Both breasts are exposed since the architecture of the breast varies in different patients and in the same patient at different periods.

FIG. 3. General setup.

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